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EXPERIENCES WITH THE PENNINGTON DIET IN THE MANAGEMENT OF OBESITY

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OBESITY in the human has been widely studied by such authorities as Newburgh and Rony.[1, 2] It is generally accepted that fat in excess will be laid down only if food intake exceeds energy output. The treatment of obesity has generally followed this premise. Diets deficient in calories have been prescribed so that caloric intake does not exceed energy output. Weight loss should automatically follow when the instructions are faithfully followed. Indeed formulae have been devised to predict the loss in weight on a measured low caloric intake of a candidate of known height and weight.[3] These low caloric diets are made up so as to be deficient in fat and carbohydrate and with protein at approximately 1 g. per kg. of body weight. It has been shown that weight loss can be achieved in this manner. The diet is followed and the desired results are obtained.[3] Unfortunately, it is difficult for most patients seen in clinical practice to follow a low caloric diet. The literature is replete with instances of diet failure on such a regimen. The difficulty is in part due to inability to control appetite. Anorectic agents such as amphetamine, phenmetrazine hydrochloride and bulk substitutes have been utilized as a means of controlling appetite.[4-6] These are of some value in the clinical mangement of an obese patient. Methods other than those of controlling appetite have also been applied. These include the administration of thyroid extract, the effect of regular exercise and psychotherapy administered both individually and in groups. However, in spite of all these methods, the long-term management of obesity presents many disappointments.[7-9] Patients often lose weight only to regain it after a short interval. In many, weight loss is never achieved.[10]

Means other than the aforementioned have long been sought in the control of appetite. Appetite and satiety, i.e. the satisfaction of appetite, are complex problems. The latter, satiety, is dependent upon many variables. One of the chief factors is the production of body heat by the specific dynamic action of ingested food. Protein has much the highest index in this regard, while fat has the lowest.[11] Rise in skin temperature and a resulting feeling of warmth are intimately correlated with the feeling of satiety. In fact, it has been suggested that the obese are slower in showing this rise, hence their desire for more food.[12] Another theory relating to satiety is that of the arteriovenous (A-V) glucose difference and its regulation of glucoreceptors in the brain stem. Mayer[13] feels that the glucoreceptors are the controlling centres of appetite and satiety. It is stated by others that satiety depends only on the body's caloric needs and the subsequent voluntary supply of calories.[14] A most attractive hypothesis, well documented by physiological study, is that which proposes that satiety is experienced because the stomach is full. Nervous impulses are sent out to the brain when the stomach is filling or full and the sensation of satiety results.[15] Satiety may then be related to many factors of the diet. If the bulk of food, its protein and its fat intake are increased, on the basis of some of these theories satiety may then more readily follow. Bulk, increased intake of fat and protein, and thus satiety, are not possible with the usual low caloric diet.

As a diet for achieving satiety while effecting weight loss, the low carbohydrate diet of Pennington shows some promise.[16, 17] This diet allows as much bulk as desired. It is high in both fat and protein. Such a diet meets many of the requirements for achievement of satiety. It provides plenty of protein to be used for heat production by the body. Calories are supplied by the high fat intake and filling of the stomach is achieved by the usual bulky nature of the diet. Pennington claims that his patients have lost weight on this diet with a caloric intake of 3000 calories. Another consideration is that of a fat-mobilizing hormone which has been reported to be present in the urine of patients on this type of diet. Urine extracts from such fasting patients have been shown to produce weight loss when injected into mice.[18] Unfortunately, verification of this work has not as yet been reported by others. One may anticipate that with such a diet hunger may be avoided, appetite satisfied and a measurable weight loss achieved. The diet is not easy to follow. Its most important re-

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quirement is the strict necessity of restricting carbohydrate intake to less than 50 g. per day. One may consume as much fat and protein as desired to produce satiety. Of course diets high in fat and protein, and therefore meats, are somewhat expensive. These may be out of the reach of some economic classes. Other ethnic groups long accustomed to high carbohydrate intakes, such as Italians and Chinese, may find such a diet highly unpalatable. However, most well-motivated patients are prepared to follow such a diet.

METHODS

Forty-eight obese individuals were selected. These were patients attending a private practice, an industrial medical centre, or the outpatient clinic of a hospital. All expressed a desire to lose weight. A copy of the diet was given to each patient. The diet was made up to allow protein and fat *ad libitum*. However, the carbohydrate component was carefully restricted to less than 50 g. per day. The object of the diet was to provide as much bulk as desired but at the same time to limit sharply the carbohydrate intake. These basic points were outlined to each patient. There were no other diet restrictions. Copies of the diet were mimeographed along with suggested menus for each meal. The patients were instructed regarding the approximate values of the usual daily foodstuffs. The high protein and high fat content foods were selected as being most useful for this type of diet. The whole regimen was reviewed with the patient after the diet had been followed for some weeks, so as to correct any misunderstanding that might have arisen. The patients at the outset found the concept of an *ad libitum* diet difficult to understand. However, with time they realized that the guiding principle of the extremely low carbohydrate intake (less than 50 g. daily) had first to be strictly maintained. They could then realize satiety by taking as much fat and protein as required.

The patients' weights varied from 140 lb. in a young woman whose height was 58 in. to 274 lb. in an elderly woman 70 in. in height. The patients ranged in age from 16 to 62 years. They all fulfilled the true definition of obesity, being 20% more than the ideal (provided by the Metropolitan Life Insurance tables[19]) weight for their height. Their weights were checked at monthly intervals for three months to one year. A small group, eight patients in all, were followed up for a two-year period. One patient was studied while in hospital and balance studies are available in this case (Fig. 1).

The patients served as their own controls, since all had been on a low caloric diet without measurable success. At least half had used anorectic agents, seven patients had taken bulk substitutes, and eight had participated in group psychotherapy for a period of eight months. None of them showed a sustained loss of weight.

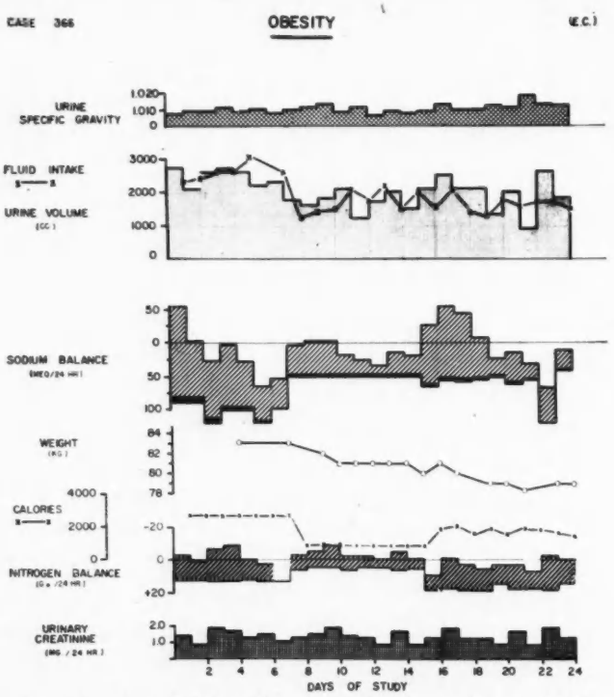

Fig. 1.—Female E.C., Level O denotes balance. Indices above the line indicate negative balance; indices below, positive balance. Day 1 to 7: 2800 cal. Weight stationary 83 kg. Positive sodium and negative nitrogen balance. Day 7 to 15: 1000 cal. Weight loss of 3 kg. Positive sodium and negative nitrogen balance. Day 15 to 24: Approx. 2000 cal. Weight loss of 1 kg. Negative sodium and positive nitrogen balance.

RESULTS

Forty-eight patients were seen initially. Of these, eight rapidly lost interest and did not wish to carry on with the diet after the first month. All of these patients complained, nonetheless, of the monotony of the diet, its constipating effect, the absence of taste and its failure to satisfy their desire for sweets. Of the remaining 40 patients, 12 felt that they were following instructions faithfully but did not lose weight. The remaining 28 patients achieved satisfactory weight loss during the period of at least six months in which the diet was followed. This loss varied from 10 to 40 lb., averaging 1½ lb. per week. Nine of the 28 patients who lost weight were able to reduce their weight to ideal chart indices.[19] The others, although showing considerable weight losses during the period of study, did not reach this desired level. Results in the single case under balance study are shown in Fig. 1.

The balance study was carried out on a woman (E.C.) who initially weighed 83 kg. (182 lb.). She was allowed a free diet, for the first seven days. It will be noted that the caloric intake was approximately 2800 calories and that little change in weight occurred. There was a substantial fall in weight from day 7 to day 15 when a low caloric diet of 1000 calories was taken. The high protein and fat diet of Pennington with only 50 g. of carbohydrate was followed for the final period from day 15 to day 24. The caloric value during this period was in the neighbourhood of 2000. There was a weight loss of at least 1 kg. (2.21 lb.) and, interesting to observe, a negative nitrogen balance and a positive sodium balance.

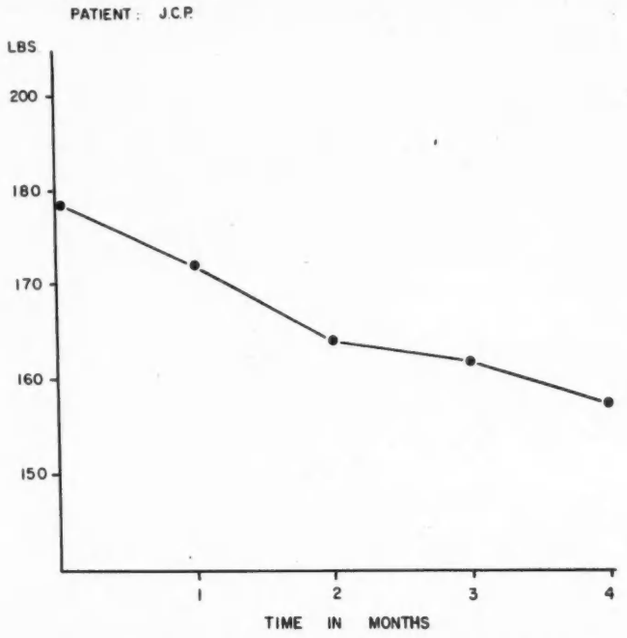

Fig. 2.—Male J.C.P., weight loss monthly of approximately 4 lb., with total fall of 16 lb.; from 178 to 160 lb., in four months.

The patients who did achieve weight loss showed a substantial fall as illustrated by a representative case (Fig. 2). All patients, including those who dropped out of the study, expressed similar opinions regarding the diet. They agreed that it was monotonous and constipating. Many missed sweets and the oral satisfaction derived from sweets. However, none of the patients experienced hunger, since they were free to eat protein and fat at will. Hunger had been a factor to most of them on low caloric diets and they were quite familiar with this form of nagging discomfort. The new diet was preferred by them, if only for this reason. The eight patients followed up for two years maintained their weight loss while following the diet.

DISCUSSION

The treatment of the obese patient has followed a stereotyped pattern for the past 20 years. Prescribing a simple low caloric diet and sympathetic handling of the patient, the usual method, had not been a rewarding form of clinical treatment. Usually, the patient was disturbed by a continual gnawing sense of hunger.[6] Attempts to overcome the feeling of hunger by the use of anorectic drugs and bulk substitutes have been found of value for limited periods.[4, 5]

The use of food high in protein and fat in order to overcome hunger does not at first glance appear to be a likely treatment for obesity. However, such a diet, high in protein and fat but low in carbohydrate, has been suggested by Pennington, who has reported that weight loss can be achieved by such means.[16, 17] Pennington also has submitted the following theory in an attempt to show that fat and carbohydrate are metabolized in a different manner by obese as compared to normal subjects. A partial block in carbohydrate metabolism at the pyruvic acid level is postulated. Pyruvic acid becomes converted to fat. Glucose intake is increased in an attempt to overcome the block. Obesity results because of the increased intake and consequent fat deposition. By inhibiting glucose intake in the obese, Pennington feels that energy will be derived not from glucose but from fat (ketogenesis). Weight loss in the obese on such a diet is achieved through fat breakdown. The evidence for this theory is hardly complete.

Our results do show that satisfactory weight loss may be accomplished by a full caloric, low carbohydrate diet. The patients ingested protein and fat as desired. Careful attention was paid to keeping carbohydrate intake to a minimum. It has been suggested that the diet was unpalatable and the caloric intake was unconsciously restricted for this reason, although the bulk may have appeared to be sufficient.

Another criticism might be that even if the total bulk and caloric intake were ingested, complete absorption may not have taken place. The answer to these points may be discussed in the light of the work of Kekwick and Pawan,[20] who have shown that obese patients will lose weight with diets of 1000 calories. Surprisingly, the rate of weight loss was increased when the composition of the diet was altered from the usual low caloric one to one predominantly made up of fat or protein. They also showed that more liberal diets, of approximately 2000 calories, sufficient to maintain an even weight in obese patients, would result in weight loss if this same caloric intake was altered to a high fat or high protein content of similar caloric value. Balance studies performed during the period showed that complete absorption occurred during the period of high fat or protein ingestion. They suggested that some aspects of metabolism are different in the obese as compared to the normal and that alteration in composition of food may alter energy output in the obese. Our results are compatible with these findings.

The same studies have been extended by Pilkington,[21] whose group has shown that obese patients on 1000 calorie diets consisting mainly of fat or protein, for long periods of time, lost weight at a constant rate. They found that after an initial rapid weight loss a steady state was achieved if the diet was continued for a sufficiently long period, usually months. The weight loss paralleled that seen in the usual isocaloric 1000 calorie diet consisting mainly of carbohydrate. One must bear in mind that these were 1000 and not 2000 calorie diets.

The detailed study on the single patient described in this report shows that weight loss occurred on a full caloric intake, consisting of high fat and protein and low carbohydrate content. The sodium balance was positive and the nitrogen balance negative during the periods of free diet and low caloric diet. However, while on the Pennington diet the sodium balance was negative and the nitrogen

balance was positive. Although one is tempted to attempt it, it is not possible to interpret these findings decisively. Shifts in mineral balances are commonly observed phenomena in the obese when the caloric intake is manipulated.

The patients who were successful in losing weight all did so on a liberal diet which prevented hunger and provided for satiety. All the other methods of weight reduction mentioned earlier have been utilized by the author in the past. The diet discussed was found to be the most satisfactory of all these methods in our hands. Weight reduction occurred dramatically with a rapid fall early and then proceeding slowly but surely. Only nine of the 28 were able to reach ideal weight indices.[19] The others did not do so well but did achieve significant weight losses. It is our feeling that the usual low isocaloric diet would be necessary to bring these remaining 18 subjects down to ideal weight indices, but this is not an established fact. As stated, the patients found this method of losing weight superior to others. They did not suffer from hunger, felt satisfied most of the time and were free to reach for food at any time. They found this to be of immeasurable comfort and thus they were able to lose weight to a greater degree and for a longer period of time than they had heretofore realized. The results reported indicated that a greater number of patients will follow such a diet for a long period with satisfactory achievement levels.

SUMMARY

Twenty-eight of 48 patients succeeded in losing weight on a liberal caloric diet high in protein and fat and low in carbohydrate, as proposed by Pennington.

The results are discussed in the light of recent metabolic studies in obesity by Kekwick and Pawa.

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THE PATHOLOGY OF DIABETES MELLITUS

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THE CONCEPTS advanced in the following presentation are based on data which, in some cases, are not yet established as conclusive fact, and which could in certain instances be queried with equal validity by other published reports not included in the references. It is felt, however, that publication of these concepts may provoke further critical analysis and bring forth a more complete understanding of the complex interrelationships involved not only in diabetes mellitus but also in normal cellular metabolism.

The syndrome diabetes mellitus is best discussed in the light of the knowledge of the functions of insulin. For the most part, medical attention has been focused on the alterations in glucose metabolism occurring in insulin deficiency. While it has been known that changes in fat and protein metabolism are involved in diabetes mellitus, these changes were thought to be consequent on abnormal glucose metabolism. It is now appreciated that insulin is directly involved not only in the synthesis of carbohydrate from glucose but also in the formation of fatty acids,[2, 7, 10] neutral fat,[2, 7, 10] aminoacids,[13] and protein.[13] To illustrate, the childhood total diabetic without insulin is a thin malnourished individual who will not grow even with adequate growth hormone and thyroxine. Conversely, short-term overaction of insulin causes hypoglycemic shock with regard to carbohydrate metabolism, while prolonged overaction results in obesity and gigantism in terms of fat and protein metabolism. Thus, insulin is involved in the synthesis of fatty acids, neutral fat, aminoacids, protein, carbohydrate and combinations of these substances such as mucopolysaccharides[1, 23] (Fig. 1). It is also responsible for the intracellular and extracellular migration of potassium ions in conjunction with formation and decomposition of glycogen.[23] From this it is apparent that the whole of the anabolic phase of body chemistry is dependent on the activity of this one physiological substance. Most important of all, the regulation of insulin action determines the balance between synthesis and destruction of tissue substances. It is the purpose of this presentation to advance the concept that it is the failure of the body servo-mechanisms that maintain this balance which is responsible for the signs and symptoms of diabetes mellitus.

Variations in the level of blood glucose have been used as a measure of the activity of circulating insulin. While values of blood glucose do reflect changes in carbohydrate metabolism, it does not follow that changes in protein or fat metabolism are affected equally or in proportion. Abnormalities in fat and protein metabolism, as exhibited by diabetic nephropathy and neuropathy, have been reported in cases presenting only mild disturbance of carbohydrate metabolism as evidenced by glucose tolerance studies.[3, 8] With our present state of knowledge, however, the level of blood glucose must serve as a guide to the sufficiency or insufficiency of insulin action in the other synthetic pathways, recognizing at the same time its lack of necessary correlation.

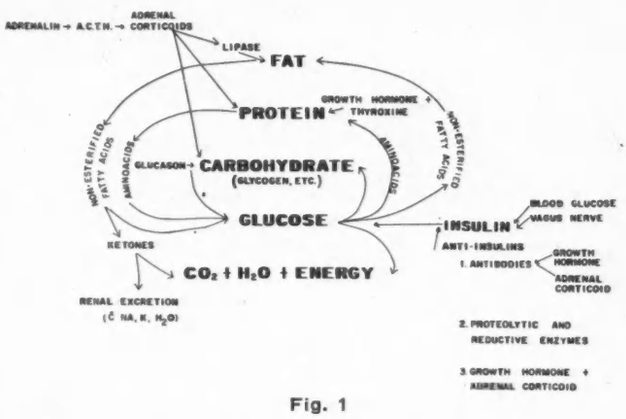

Fig. 1

The question arises as to how one biological chemical can perform in so many different reactions. It has been suggested that insulin acts primarily on transport systems, located in cell membranes and intracellularly.[17] The availability of coenzymes, which function as transport agents within the cell, is determined by reduction of receptor groups on their molecules. The action of insulin may be to alter each of these different coenzymes by a common metabolic step, namely reduction, and thus be involved in diverse and apparently unrelated biochemical reactions.[18]

The elaboration of insulin by the islets of Langerhans is under the influence of three variable factors: firstly, the level of blood glucose;[19] secondly, the vascularity of the islets as regulated by nervous stimuli;[23] and finally, the activity of islet-cell glucose-6-phosphatase.[22] The latter enzyme makes free glucose available to the islet cells. As long as the enzyme is functional, insulin is apparently formed. It has been postulated that the sulfonylurea compounds act by preventing the degradation of this enzyme, augmenting insulin output by islet cells.[22]

The secretion of insulin and the functional activity of insulin are not synonymous terms. It is recognized that the regulation of synthetic processes from blood glucose by changing the quantity of circulating insulin is a coarse, cumbersome mechanism, fairly slow to activate or depress. For finer control of insulin action, antagonists, inhibitors and insulinases are provided which are more rapidly effective than is reduction of insulin secretion.[12]

Insulin inhibitors are substances which either bind the insulin molecule, such as antibodies,[17] or compete successfully for the sites of insulin action.[21, 24] Growth hormone and adrenal corticoids are examples of the latter.

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Insulin antagonists are substances which reverse the physiological action of insulin: adrenaline and glucagon release glucose from glycogen. Adrenal corticoids mobilize fatty acids and aminoacids from neutral fat and protein respectively.[20]

Insulinases are enzymes primarily found in the liver, which destroy insulin either by reduction or by proteolysis.[21, 24] The circulating half-life of insulin has been demonstrated to be approximately 40 minutes,[24] its removal from the blood stream being partly carried out by insulinases.

In view of the interplay of these numerous factors which may alter either secretion or action of insulin, the classification of causes of the diabetes mellitus syndrome is a complex one. The effectiveness of these factors may be temporary or permanent, providing intermittency of symptoms to complicate further both diagnosis and treatment of the syndrome.

Classification of Diabetes Mellitus

A. Hypoinsulinism
1. Islet cell failure
   (a) Congenital hypoplasia of islets
   (b) Induced
1–Excess glucose intake
2–Dehydroascorbic acid } Experimental
3–Alloxan
4–Excess pituitary growth hormone
5–Excess adrenal corticoids
   (a) Spontaneous (adenoma, carcinoma) (Cushing's syndrome)
   (b) ACTH or growth hormone stimulation (Cushing's disease)
6–Pancreatic destruction
   (a) Hemochromatosis
   (b) Pancreatitis
   (c) Primary or metastatic malignancy
7–Pancreatectomy
8–Glucagon-secreting islet-cell tumour of pancreas
9–Obesity
B. Insulin antagonism
1. Excess ACTH or growth hormone
   (a) Primary pituitary hyperfunction
   (b) Pituitary adenoma (eosinophil)
   (c) Hypothalamic stimulation (tumour, inflammation)[11]
2. Excess adrenal corticoid hormones
   (a) Primary (Cushing's syndrome)
   (b) Secondary (ACTH or growth hormone) (Cushing's disease)
   (c) Extrapancreatic malignancies
      1. Lung 2. Ovary 3. Thymus
3. Adrenal medullary tumour (pheochromocytoma)
4. Insulin-binding antibodies
5. Insulinase hyperactivity
6. Glucagon-secreting islet-cell tumours

Classification of the causes of diabetes is an important procedure; clinically, over 90% of all diabetics fall into three main groups.

The growth-onset or "juvenile" diabetic, who constitutes about 5% of all cases, is said to have advanced bone age and dentition, suggesting overstimulation by pituitary growth hormone.[5] Assay of the pancreas for insulin in this group reveals almost total depletion of insulin.[18] The male to female ratio is approximately one to one. Symptomatically the diabetes in this group is more labile or "brittle", reflecting the presence of insulin-binding antibodies which may be readily dissociated from the insulin molecule by endogenous release or exogenous administration of cortisone. Both ketosis and insulin shock are more prevalent owing to fluctuations in active insulin brought about by variations in diet, exercise or spontaneous antibody binding of insulin. Other complications such as arteriosclerosis, nephropathy, neuropathy and retinal disease are more common in this group.[4, 23] These findings are said to be related to the difficulty in maintaining metabolic balance.[4, 23]

The second group is the largest, constituting over 80% of all cases of diabetes. It is composed of obese individuals over 40 years of age, women predominating over men by a ratio of two to one. The pancreas in this group contains on the average approximately half of the insulin found in the normal pancreas.[19] Reduction in body weight to normal or subnormal levels results in remission of the diabetic syndrome.

To explain the etiology of diabetes mellitus in this group, it is acknowledged that insulin is required for the synthesis of glycerol from glucose[25] and neutral fat from glycerol and fatty acids.[2, 7, 10] Since neutral fat in storage depots in the omentum and subcutaneous tissues is not a static substance but is being broken down to fatty acids and reconstituted to neutral fat continuously,[25] the more fat an individual possesses, the more insulin is required for this purpose. As an indication of the rate of fat catabolism and anabolism, the half-life of circulating non-esterified fatty acids is only two to three minutes.[30] It follows that reduction of fat stores releases insulin for other functions and therefore symptoms of the syndrome subside.

The third group of individuals presenting with diabetes mellitus are similar to the second in age and sex ratio, and usually are obese or give a history of previous obesity. Clinically their diabetic symptoms resemble those found in patients in the "juvenile" group. Characteristically, the content of insulin in the pancreas is comparable to the level found in the "juvenile" group.[19] They too have fluctuant ketosis with episodes of hypoglycemia. This group is small, totalling an additional 5% to 10% of all diabetics.

Having discussed the etiology and pathogenetic mechanisms involved in diabetes mellitus, the pathologic alterations in body tissue produced by a failure of insulin action merit attention. The changes that arise are related to either acute or chronic insulin insufficiency. Since there is no evidence to the contrary, it is suggested that the

majority of the late complications of diabetes are the result of the same changes that occur in the acute phase of insulin insufficiency but are more subtle and prolonged.

Acute insulin lack produces the syndrome of diabetic ketosis. Unlike some lower animals such as the dog, man can not exist on fatty acids as a source of energy. The enzyme systems which normally use ketone bodies for quick energy production are flooded with substrate in diabetic acidosis.[29] To maintain blood pH at an optimum level, the ketones which have accumulated in the blood stream are excreted via the urine along with precious quantities of neutralizing sodium and potassium ions. When stores of these basic ions have been depleted, the increasing acidosis acts as a cerebral depressant, resulting in "diabetic coma". The blood glucose level reaches a high value and is derived from glycogen and protein stores. The renal threshold for glucose is exceeded relatively early with a constant outpouring of urine laden with tremendous quantities of potential energy as well as excessive volumes of water.

In discussing the complications of latent insulin insufficiency, it is useful to consider that the disruption of tissue integrity by the mobilization of fat, protein, and polysaccharides to form glucose and ketones occurs in a similiar but less pronounced fashion. It is theoretically possible but highly improbable that tissue catabolism and anabolism are always in balance when insulin is self-administered. The fact that fluctuations undoubtedly occur makes it requisite to consider such fluctuations involved in the pathogenesis of the abnormalities known to be the chronic complications of this disease.

Numerous conditions described in elderly people are called "degenerative diseases" and are attributed to "wear and tear". "Degeneration" is present whenever changes have occurred which impair normal function. Arteriosclerosis is one such pathologic process. It is accelerated in the presence of hypertension, idiopathic hyperlipemia and diabetes mellitus.[14, 15] Substances within the vessel wall which may be altered chemically in the diabetic syndrome are the mucopolysaccharides of the ground substance as well as the protein of smooth muscle and elastic tissue. The degree of hydration of the vessel wall may be altered by the migration of basic ions. Whether such changes are responsible for the fundamental abnormality in arteriosclerosis is not known, but certainly they may contribute to it.[23, 26]

Diabetic nephropathy is a clinical entity characterized by changes in the renal glomeruli. The earliest lesion is a hyaline thickening of the basement membrane of the glomerular endothelium.[9] The hyalinization results from the deposition of a lipoprotein complex. It may give rise to two varieties of lesion, one nodular and the other diffuse. The reason for this site is unknown.[14]

Retinopathy is found in approximately 85% of patients with diabetic glomerulosclerosis. Retinal aneurysms are formed by the ballooning-out of segments of capillary wall which have been infiltrated by lipid material.[16] Hemorrhage from these weakened zones is followed by organization of the exudate, new blood vessel formation, scar tissue formation and, finally retinal detachment.[23]

The neuropathy of diabetes has been ascribed to either arteriosclerosis or a nutritional disturbance. Evidence for the latter is the demonstration that a high fat diet increases the body requirements for folic acid, vitamin B_{12} and methionine.[27, 28] Some patients respond to the administration of vitamin B_{12}.[5]

The predisposition of diabetics to infections such as tuberculosis, furunculosis, moniliasis, mucormycosis and acute pyelonephritis is well known.[6] Elevation of blood glucose is not a prerequisite; rather, change in blood pH with acidosis facilitates this complication.[6]

Diabetic individuals have a higher than normal incidence of gallstones which is thought to be related to susceptibility to infection as well as to hypercholesterolemia.[23] Other stigmata of disordered fat metabolism are the lipoid infiltrations seen in the skin and spleen.[23] The hyalinization noted in the islets of Langerhans is not of etiologic significance in this disease nor is it pathognomonic, although it is more frequent in diabetics.[23]

SUMMARY

The pathologic physiology and anatomy of diabetes mellitus have been described and discussed in relation to the failure of the servo-mechanisms which regulate the synthetic action of insulin. While the concepts advanced in this paper have not been conclusively established, it is hoped that their presentation will be a stimulus for both further thought and research.

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GAS GANGRENE FOLLOWING PERFORATION OF THE ALIMENTARY CANAL
REPORT OF FOUR CASES*

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CLOSTRIDIA may be recovered from almost any sample of soil,[1] and are presumably often ingested by mouth. They multiply in the intestinal tract, and may be readily recovered in the feces.[1] However, they rarely prove pathogenic if confined to the intestinal tract,[2] perhaps because there they produce only small quantities of their toxins, or because their toxins are destroyed by enzymes. Goudie[3] has shown that a proteolytic enzyme recovered from human feces destroys the alpha toxin of *Clostridium welchii*, and Goudie and Duncan[4] have suggested that this may be one of the reasons the organism is not pathogenic in the gut. One would expect, nevertheless, that if pathogenic clostridia escaped from the bowel into the tissues an infection would become established. It is therefore surprising that this so rarely occurs.

Clostridial infections are uncommon after elective surgery and rare after intestinal perforation, even in cases with peritoneal contamination. Thirteen per cent of Millar's[5] 607 cases of gas gangrene encountered in civilian practice developed this infection after elective surgery, but he does not mention any case occurring as a complication of intestinal perforation. Callander, Haim and Maximow[6] do cite a case secondary to perforation, but do not include perforation of the gut in their list of factors predisposing to gas gangrene. Other reports of gas gangrene secondary to intestinal perforation are few. Warthen[7] reported three cases and others have mentioned single examples.[8-11] The present report adds four new cases of gas gangrene secondary to perforation of a viscus, which occurred among 8190 autopsies over an 18-year period, and discusses why this complication is so rare.

CASE REPORTS

CASE 1.—A 71-year-old mildly diabetic house wife was admitted to hospital complaining of pain and swelling in the right leg. A gallbladder series had been done a month before, after the patient had had several vomiting attacks, but had shown no abnormality. The evening before admission, the patient became nauseated, vomited and developed a fever. Next morning, the toes and calf of her right leg suddenly became pale and painful. Treatment at home with hot water bottles and compresses brought no relief. The leg became swollen and mottled and within a few hours developed skin blisters. Severe pain forced the patient to go to hospital. On admission she was pale and sweating profusely, and complained of pain in her right leg. Her temperature was 98° F., pulse 100/min., respiratory rate 36/min., and blood pressure 140/80 mm. Hg.

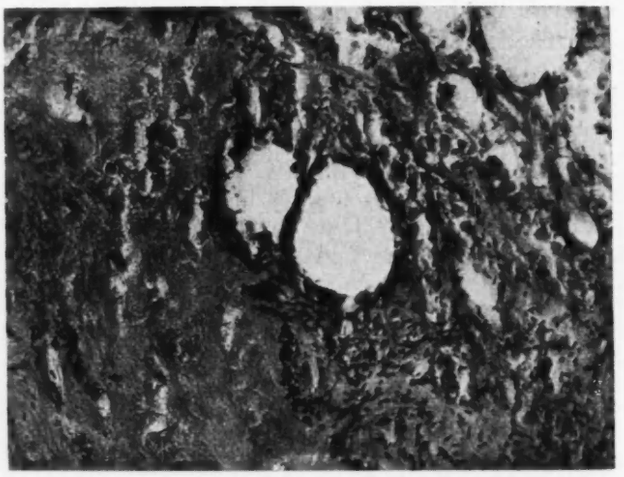

Fig. 1.—Case 1. Clostridia and gas bubbles in pericecal tissues (Gram, × 400).

Occasional basal rales were heard. Marked abdominal guarding prevented satisfactory abdominal examination. Rectal examination was normal. The pale right leg showed bluish-black mottling, and was cold, tense and tender. Two large blisters filled with reddish fluid were found on the thigh. In the emergency department, crepitation was noted in the lower leg only, but in the ward, subcutaneous crepitation was palpable from foot to the anterior thigh. Only the inguinal femoral pulse could be felt on that side. The hemoglobin value was 11 g. %; the white blood cell count 25,600 per c.mm. Urine analysis showed 2+ sugar, but no albumin or ketones.

A diagnosis of gas gangrene was made. The patient was given 500 mg. of chloramphenicol and was taken to the operating room for a right supracondylar amputation. Wide incisions were left in the stump. She died at the end of the operation, 13½ hours after the onset of pain in the leg.

POSTMORTEM FINDINGS

Gross.—The autopsy was confined to the thorax and abdomen and was performed nine hours after death. On opening the abdomen, a mass the size of a grapefruit was found in the right iliac fossa. It was made up of edematous omentum, terminal ileum and cecum, bound together by thin fibrinous adhesions. A fungating, necrotic carcinoma, 9 cm. in diameter, extended from the posterior wall of the cecum into the ileo-cecal valve. It had metastasized to regional lymph nodes. The anterior cecal wall proximal to the carcinoma was thinned, necrotic and friable. Acute peritonitis was marked in this area. The cecum was retroperitoneal and rested on the right iliopsoas muscle. Posteriorly, cecum and muscle were united by inflammatory exudate. The iliopsoas was plum-coloured, friable and crepitant, and on pressure exuded a gas without noticeable odour. Palpable crepitation extended into the anterior abdominal wall. The muscles of the stump of the amputated leg had much the same appearance as had the iliopsoas, except that they were pale pink in colour. No occlusion was found in the leg vessels.

Microscopic.—The tumour of the cecum was an anaplastic adenocarcinoma. Many stout Gram-positive bacilli were seen in the cecal wall near the carcinoma and in the muscles of the pelvis and leg. The voluntary muscle fibres showed marked degenerative changes. Nuclei were absent or fragmented; brightly acidophilic

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cytoplasm contained many small droplets of fat. Edema and focal hemorrhages were marked in perimysial connective tissue, but there was only a scant polymorphonuclear response. Occasional cystic spaces, presumably gas bubbles, were seen between the widely separated muscle fibres. Other findings included a small adenomatous polyp of the cecum 2 cm. distal to the carcinoma, marked cloudy swelling of liver and kidneys, mild atrophy of the islets of Langerhans and generalized arteriosclerosis.

Bacteriology.—*Clostridium septicum* was cultured from the leg before death, and from pelvic and paracecal swabs taken at autopsy.

CASE 2.—A 51-year-old man underwent a partial gastrectomy and gastrojejunostomy for pyloric stenosis nine years before his final admission. He was readmitted because of symptoms suggesting stomal ulceration. After a period of medical treatment, the ulcer was excised and a new gastrojejunostomy fashioned. Fourteen days later, the patient complained of dysphagia, which gradually worsened. Esophagoscopy did not show a lesion, but bougies were passed. The following day, a barium-meal examination showed barium in the retroperitoneal space. Twenty-four hours later, radiographs showed gas in the posterior mediastinum. The patient died four days later. During the last days of his illness, he had persistent tachycardia and fever, and developed jaundice. His blood pressure collapsed in the final stages.

POSTMORTEM FINDINGS

Gross.—The autopsy was performed 2½ hours after death. The body was moderately jaundiced. No cause could be found for the dysphagia. The gastrojejunal anastomosis was well healed and admitted two fingers. The œsophagus was perforated just above the cardia, and from a small recess a sinus tract led to necrotic, crepitant retroperitoneal muscle. When this was sectioned, foul gas was released. The muscular necrosis was extensive, involving the retroperitoneal muscles and extending on to the anterior abdominal wall.

Microscopic.—The necrotic muscle fibres of the psoas and diaphragm were separated by edema and hemorrhage. Occasional polymorphonuclear leukocytes were present, as were Gram-positive cocci and stout Gram-positive rods. Other findings included multiple small pulmonary emboli, acute bronchopneumonia and serofibrinous pleurisy.

Bacteriology.—Heart blood and retroperitoneal swabs gave a heavy growth of *Cl. welchii* and *E. coli* and a light growth of beta-hemolytic streptococci of Lancefield group A.

CASE 3.—This 65-year-old man had experienced malaise for a day before he suddenly developed abdominal pain, which was at first epigastric but later became generalized. He was known to have had a gastric ulcer for four years. When admitted to hospital, he was in shock; bowel sounds were absent and his abdomen had a board-like rigidity. His hemoglobin value was 95% and his white blood cell count was 20,000 per c.mm. Laparotomy, performed shortly after admission, confirmed the perforation of an anterior pyloric ulcer. The hole was closed by omental flap, but the patient died the next day.

POSTMORTEM FINDINGS

Gross.—Autopsy, performed five hours after death, revealed a large peptic ulcer, 8.5 x 2.5 cm., which straddled the lesser curvature near the pylorus. There was a generalized acute peritonitis with loculation of pus. The right rectus muscle was crepitant from the operative incision to the pubis, as were the tissues of the flank above the right inguinal ligament, and the lower one-third of the left rectus abdominis. The affected muscles appeared necrotic and partially liquefied. Incidental findings included marked red staining of the vascular intima and an aortic thrombus immediately above the bifurcation. A small rectal carcinoma was also found.

Microscopic.—Sections from the affected muscles showed fibres in all stages of degeneration, with marked edema but few polymorphonuclear leukocytes in the connective tissue.

Bacteriology.—A heavy growth of *Cl. welchii* was obtained from swabs of the peritoneum taken at operation and also from swabs of the rectus abdominis taken at autopsy.

CASE 4.—A 53-year-old man was admitted to hospital complaining of generalized abdominal cramps with dull, left loin pain of seven months' duration, and urinary frequency of two months' duration. He had lost 40 lb. in weight. On examination, tenderness in the left loin was the only significant finding. Cystoscopy showed a hyperemic bladder mucosa suggestive of a lower bowel lesion. Further investigation was prevented by the sudden onset of abdominal distension and severe colic. A flat radiograph of the abdomen confirmed the diagnosis of large bowel obstruction. Laparotomy revealed a small perforation above a sigmoid mass, and generalized peritonitis. A cecostomy was created and abdominal drainage begun. The patient deteriorated steadily, with evidence of persistent intestinal obstruction. On the 5th postoperative day, the wound edges were noted to be reddened and crepitant. The cellulitis spread slowly, and after two days was incised and drained. It appeared to respond to treatment during succeeding days. The final stage of the illness was heralded by jaundice and a rising temperature and pulse rate. He died 26 days after the operation.

POSTMORTEM FINDINGS

Gross.—A biopsy of the mass in the sigmoid taken at operation had shown necrosis and acute inflammation in fat and fibrous tissue, with numerous Gram-positive rods free in the tissue. This observation was compatible with the clinical diagnosis of perforated diverticulum. However, at autopsy performed three hours after death, it was revealed that the lesion was an adenocarcinoma. The tumour was found in an inflammatory mass the size of an orange which included necrotic segments of the lower descending colon and sigmoid. The site of perforation in the descending colon proximal to the carcinoma could still be defined. The muscles of the abdominal wall appeared normal, but the tissues at the edges of the drainage wounds showed acute inflammation and focal necrosis.

Bacteriology.—*Cl. welchii* was cultured from the pus in the abdominal cavity at the time of operation, and later from the anterior abdominal wall muscles.

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DISCUSSION

The gut serves as a reservoir of clostridia, and bacteria must easily gain entry to the peritoneal cavity when the gut is ruptured. Jennings[12] found that *Cl. welchii* could be cultured from 90% of acutely inflamed appendices, and could be recovered from the abdominal fluid in 67% of cases. It is therefore surprising that gas gangrene, such as occurred in the cases reported here, so rarely follows intestinal rupture.

Probably several factors are important in preventing the development of gas gangrene in such cases. Not all clostridia are pathogenic. Different varities of these pathogens are common in different parts of the world, but *Cl. welchii* Type A, *Cl. oedematiens*, *Cl. septicum* and *Cl. histolyticum*, either singly or in combination, are responsible for the majority of cases of clinical disease. Or again, pathogenic bacteria may contaminate an area but not proliferate. MacLennan[13] reported that 20-30% of war wounds were contaminated by pathogenic clostridia, but only 1.5% developed gas gangrene, and 5% anaerobic cellulitis. The strict anaerobic requirement of these organisms may be the most important factor limiting growth. As is well known, necrotic tissue and the presence of certain synergistic bacteria favour the growth of clostridia, probably by reducing the oxygen tension. If infection does become established in the muscle, it spreads rapidly, aided by gas and toxin production.[14]

The histological changes seen in affected human muscle were well described in Robb-Smith's[15] study. He found that the muscle fibres at the advancing edge of the lesion had a greater affinity for eosin. Their nuclei had usually disappeared, but occasionally fragments of nuclear material persisted. Myofibrils and cross striations were usually preserved. Fat droplets appeared in the cytoplasm, but this change was not specific. The muscle fibres became separated by edema of the endomysial connective tissue. The edema contained very little fibrin, and was less basophilic than usual, possibly because of its low protein content. Often many clostridia were found in it. The polymorphonuclear leukocyte response was sparse, and those neutrophils which did migrate into the tissues were destroyed rapidly. Areas of hemorrhage were seen, but often erythrocytes appeared as ghost cells, because of loss of their hemoglobin content. Nuclei of the connective tissue cells usually underwent karyolysis, as did the nuclei of the muscle cells, but were sometimes preserved despite extensive muscle changes. The reticulum membrane continued in close apposition to the sarcolemma, and was not grossly altered at the spreading edge of the lesion. Small vessels contained fat droplets, degenerated erythrocytes or leukocytes, or fibrin thrombi. The perivascular tissues were edematous. Nerves showed edema of their connective tissue. Acute inflammatory cells might be more numerous in the vicinity of nerve fibres.[16] Cysts representing gas bubbles were seen in the perimysial tissue. Fat had usually disappeared from local depots but occasional disrupted fat cells could be found. In more severely damaged muscles, Robb-Smith described rupture and distortion of muscle fibres. Surprisingly, myofibrils could be demonstrated despite advanced muscle breakdown. The reticulum network became separated from the sarcolemma and its fibrils diminished in number. Those remaining were often fragmented. Collagen fibres also disappeared, but elastic tissue seemed little affected. The first two cases here described showed these changes and some of these features are demonstrated in Fig. 2.

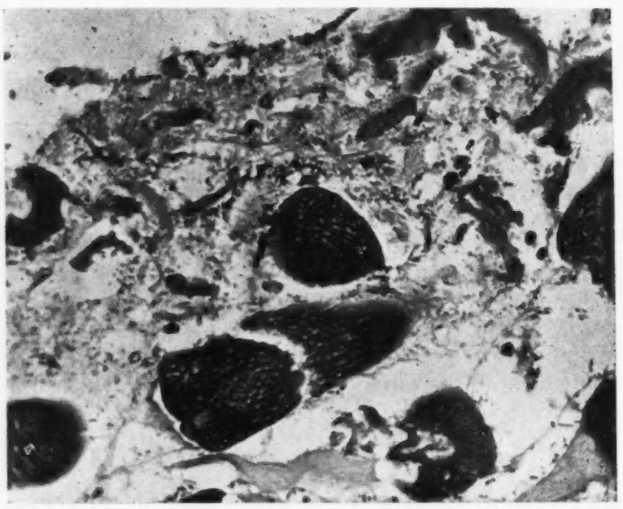

Fig. 2.—Case 2. Clostridial myositis affecting the psoas muscle. Note bacteria, scanty acute inflammatory cell exudate, edema and degenerative changes in muscle (H. & E., × 400).

Although the clinician has as yet no method of determining whether clostridial contamination will lead to infection, it has become clear that certain types of wounds are more likely to be complicated by gas gangrene. Among the more dangerous are those in which the blood supply is disrupted; those which contain devitalized muscle; those containing foreign bodies; and puncture wounds, particularly of the thigh, calf or buttock.[17] In such cases, prompt prophylactic treatment with early debridement and administration of antibiotics is most desirable. If, despite these precautions, infection is established, it may not be apparent at once. The early changes are unfortunately not specific. The wound may suggest a pyogenic rather than a clostridial infection. However, sometimes the signs do suggest clostridial infection. The wound may leak a dirty, watery, brown fluid, with or without the characteristic odour. The overlying skin may be white, shining and tense, though often it remains essentially normal.[18] Vesicles, changes in skin colour, and palpable crepitation are usually late signs. It should be emphasized that palpable crepitation is not necessary for diagnosis. Indeed, Lindsey's[19] experimental work has shown that toxemia is usually profound by the time crepitation is obvious.

In the particular type of infection under consideration here, gas gangrene secondary to intestinal perforation, none of these warning signs are avail-

able, for there is no external wound. Other signs and symptoms therefore become most important, for early diagnosis is imperative. Altemeier *et al.*[18] in their review list the following signs and symptoms as aids to early diagnosis. The patient appears pale, almost grey; perspires profusely; feels weak; and complains of severe pain in the affected area. He is apathetic, and may be anorexic, or may vomit. The pulse is feeble and rapid. The tachycardia is not related to fever. Indeed, the patient's temperature may remain normal until death. The blood pressure is usually normal. Hypotension indicates a poor prognosis. A mild leukocytosis may be found, and there is usually a progressive anemia, due in part to hemolysis by bacterial toxins. The toxemia may be severe enough to cause jaundice. Even though palpable crepitation may not be present, gas may be detected in tissue by x-ray examination.

The first of the patients described in this paper presented with a majority of the symptoms and signs discussed. Gas presenting at a site remote from the primary lesion, as in this example, has been reported previously, and is a bad sign, all of the reported patients dying.[8, 10, 11] The discovery of gas in the tissues by x-ray examination aided diagnosis in the second case. Later the patient had persistent tachycardia and mild fever. Hemolysis caused by the alpha toxin of *Cl. welchii* produced this man's jaundice and the classical autopsy finding of red-stained vascular intima. Both patients had diffuse clostridial myositis.[17] The third case was probably another example of diffuse clostridial myositis, but the part played by the clostridial infection as a factor leading to the patient's death could not be determined. The last case may have been an example of anaerobic cellulitis.[17] This form of clostridial infection is, as this case demonstrated, the most amenable to treatment. It is not known whether the benign course is due to the fact that few bacteria proliferate or that little toxin is produced. The last two cases both had infection in the anterior abdominal muscles. This is the usual site of infection in those few cases of clostridial disease which follow elective surgery.

Thus the diagnosis of gas gangrene is difficult and too often is made only when the patient is moribund. However, if the possibility is kept in mind, the diagnosis may be suspected earlier and some patients may be saved.

SUMMARY

Four cases in which gas gangrene followed perforation of the alimentary canal are described. The modes of presentation of the disease are briefly reviewed.

I am greatly indebted to Dr. G. C. McMillan and Dr. A. C. Ritchie for help in the preparation of this paper. Mr. Harold Coletta took the photograph.

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POLYCYTHEMIA (ERYTHROCYTOSIS) AND NON-NEOPLASTIC RENAL DISEASE

REPORT OF A CASE AND REVIEW OF THE LITERATURE

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THE association of polycythemia with cerebellar hemangioendothelioma,[1-3] uterine myofibroma,[4-7] hypernephroma,[8-14] benign renal tumours,[13, 15] and less often with other neoplastic conditions, is now well documented and was recently reviewed.[16]

It is reported that in these cases splenomegaly, leukocytosis and thrombocytosis are not as frequent as in polycythemia vera;[12] on the other hand, normal arterial blood oxygen saturation differentiates them from cases of erythrocytosis secondary to anoxia.

The causal relationship between the tumour and the polycythemia first advanced by Forssell in the case of hypernephroma[8] is strongly supported by several instances of remission or cure of polycythemia which followed the extirpation of the tumour.[16]

To our knowledge, the only satisfactorily documented examples of the association of polycythemia with non-neoplastic disease are the 11 cases of unilateral and bilateral hydronephrosis or cystic disease of the kidney summarized in Table I,[11, 13, 17-21] of which 10 have been recently reviewed by Jones *et al.*[21] In six instances, polycythemia subsided

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TABLE I.—POLYCYTHEMIA (ERYTHROCYTOSIS)

Case No.	Source	Year	Author's case No.	Renal disease	Patient's Age	Patient's Sex	Mode of presentation	HEMATOLOGICAL Hb. (g. per 100 ml.)	P.C.V. (%)	Red cells (×10⁶)	Red cell volume (ml./kg.)	Blood volume	White cells (per c.mm.)
1	Kurrle	1954		Polycystic kidneys	42	M	—	144%	—	9.0	—	—	10,400
2	Cooper and Tuttle	1957		Left hydronephrosis secondary to ureteropelvic obstruction (calculus)	55	M	Fatigue, anorexia, headaches	17.9–19.0	66–68	6.8–8.2	—	7750 ml. predicted 5800 ± 600 c.c.	6400–11,300
3	Gardner and Freyman	1958		Right hydronephrosis due to obstruction of upper 1/3 of the ureter (calculus)	65	M	Thrombophlebitis	19.6–21.4	64–68	6.88–7.68	40.9	70.2 ml./kg.	11,050
4	Forsell	1958	6	Polycystic (right) kidney	61	M	Bloody stools, dysuria	116–126%	—	5.17–6.28	—	—	4500–7200
5	Forsell	1958	7	Polycystic kidneys	32	M	—	139–141% (Sahli)	70–74	7.10–8.10	—	9329 ml.	8100–10,000
6	Forsell	1958	8	Polycystic (right) kidney	61	F	Angina pectoris	134–139%	66–70	6.3–7.24	—	7480 ml. 7830 ml.	10,300 12,000
7	Forsell	1958	9	Polycystic kidneys (predominantly right)	57	M	Cerebrovascular accident	131–141%	63–71	6.7–7.42	—	8267 ml.	5500–9400
8	Lawrence and Donald	1959		Left hydronephrosis (?congenital band across ureter)	37	M	Constipation and abdominal pain	17.7–23	—	6.4–8.8	—	—	6400–10,000
9	Massachusetts Gen. Hosp. Case No. 45311	1959		Right hydronephrosis due to ureteral stricture	62	M	Subdural hematoma	21.8	67	—	—	—	10,800
10	Jones *et al.*	1960	1	Left hydronephrosis	67	M	Left hemiplegia	21.8	62	6.8	39.0	84.5 ml./kg.	9900
11	Jones *et al.*	1960	2	Right polycystic kidney	55	M	Routine examination	18.8	57	6.6	33.2	66.0 ml./kg.	13,000
12	Present case	1961	1	Bilateral hydronephrosis	50	M	Constipation and abdominal pain	17.6–19.7	55–60	5.4–6.4	40.5	84.5 ml./kg.	5800–12,550

*Adapted from Jones *et al.*[21]

after the removal of the affected kidney. The relationship between non-neoplastic renal disease and polycythemia is of interest because of the role ascribed to the kidney in either the production or activation of erythropoietin, a humoral factor (or one of the factors) involved in the regulation of erythropoiesis.[22]

Since reports of polycythemia associated with non-neoplastic renal disease are so few, it was considered of interest to report an additional case.

Mr. G.H. (University Hospital No. 23493), a 50-year-old man, entered hospital in June of 1957 because of the exacerbation of intermittent constipation of four years' duration. Apart from nocturia and some loss of muscular strength, there were no other symptoms.

On physical examination, he appeared well nourished and strongly built. His blood pressure was 130 systolic and 85 diastolic. There was a large round mass in the left abdomen and the spleen was palpable on deep inspiration. The liver did not appear enlarged, but felt firm.

His hemoglobin value ranged from 17.6 to 19.7 g. per 100 ml.; hematocrit from 55% to 60%; and white blood cell count from 5800 to 12,550 per c.mm., with a normal differential count. The platelet count varied from 270,000 to 370,000 per c.mm. and the sedimentation rate was 1 mm. in the first hour. Red blood cell volume and plasma volume were found to be increased and were consistent with the diagnosis of polycythemia (Table II).

The urine showed isosthenuria, albuminuria 20-40 mg./100 ml., and 4-6 pus cells per high power field. Urine culture was negative.

Non-protein nitrogen varied from 62 to 102 mg./100 ml. and serum creatinine from 6-9 mg./100 ml. Serum bicarbonate ranged from 11.2 to 18.2 mEq./l., but electrolytes were normal otherwise. Serum uric acid was 7.9 mg./100 ml.

No dye was excreted on intravenous pyelography. A retrograde pyelogram of the left kidney revealed displacement of the ureter by a huge hydronephrotic kidney. The right kidney was grossly hydronephrotic (Fig. 1). The ureters were not distended.

The patient improved on conservative therapy and was followed up regularly for two years after discharge. He was able to work and neither his renal function nor hematological picture showed any significant change, although he was given 2.6 microcuries (μc.) of radioactive phosphorus (P^{32}) in June 1958. His blood pressure in January 1958 was 148 mm. Hg systolic and 100 mm. Hg diastolic. He died suddenly of massive cerebral hemorrhage in August 1959.

Postmortem Findings

Autopsy showed massive intracerebral hemorrhage involving the right hemisphere with recent extension to the ventricular system, mid-brain, pons and sub-

TABLE II.—RED CELL, PLASMA AND TOTAL BLOOD VOLUME DATA

	Red cell volume ml.	Red cell volume ml. per kg. body weight	Plasma volume ml.	Plasma volume ml. per kg. body weight	Total blood volume ml.	Total blood volume ml. per kg. body weight
Normal values for male*	—	26–34	—	36–52	—	65–81
Patient G.H. Wt. 85 kg., Ht. 174 cm.	3450	40.5	3720	44.0	7200	84.5

*Normal values are based on 209 determinations carried out in the Department of Therapeutic Radiology, University Hospital, Saskatoon, Sask. Radiochromium, in the form of sodium chromate, was used for labelling of red cell and red cell volume determinations;[23] R.I.S.A. (radioactive iodinated human serum albumin) was used as a tracer substance in estimating plasma volume.[24]

AND NON-NEOPLASTIC RENAL DISEASE*

FINDINGS					RENAL FUNCTION					RESULTS OF NEPHRECTOMY			
Platelets (per c.mm.)	Bone marrow	Splenomegaly	Arterial oxygen sat.	Serum uric acid (mg./100 ml.)	Azotemia (mg./100 ml.)	GFR (ml./min.) †	Max. urine concentration	Blood pressure (mm. Hg)	Nephrectomy	Erythrocytosis remitted	Hypertension remitted	Other types of therapy	Autopsy
452,000	—	No	—	—	—	—	—	200/130	No	—	—	V‡, P^{32}	—
308,000 360,000	Normal	—	—	—	NPN 41	—	1.014	150/100	Yes	Yes	Yes	V	—
Normal	Moderate erythroid hyperplasia	No	Normal	—	—	—	1.024	190/120	Yes	Yes	Yes	V	—
146,000	Intense erythropoiesis	No	—	—	Urea 38	82	1.028	Elevated	Yes	Yes	—	—	—
Normal	Moderately hyperplastic (all series)	Yes	—	—	Urea 24	177	1.026	Elevated	No	—	—	—	—
400,000	Moderately hyperplastic (all series)	Yes	—	—	Normal	119	1.026	Elevated	No	—	—	—	—
—	Almost normal	No	—	—	Urea 40	117	1.022	Elevated	No	—	—	—	—
750,000	Erythroid hyperplasia	No	—	—	—	—	—	150/105	Yes	Yes	No comment	V, P^{32}	—
258,000	—	—	97%	2.4	NPN 37	—	—	160/110	No	—	—	—	Yes
171,000	Slight erythroid hyperplasia	No	95%	—	Urea 40–48	85	—	210/120	Yes	Yes	No comment	—	—
185,000	—	No	—	—	Urea 25	75	—	160/90	Yes	Yes	No comment	—	—
370,000	Slight erythroid hyperplasia	Yes	—	7.9	NPN 62–102	—	—	130/85	No	—	—	P^{32}	Yes

†As endogenous creatinine clearance. ‡Venesection.

arachnoid space. The heart weighed 405 g. and showed moderate hypertensive changes.

The left kidney was greatly enlarged, protruding anteriorly and displacing the abdominal viscera (Fig. 2). It weighed 3400 g. with its contents and measured 34 x 9 x 17 cm. The capsule stripped with ease. The cortical surface was lobulated, yellowish-brown and smooth. An aberrant branch of the renal vein crossed the ureteral pelvic junction to reach the lower pole of the kidney and was obstructing the flow of urine into the ureter. On section (Fig. 3), the renal pelvis was markedly dilated. The kidney consisted of multiple large and medium-sized sacs extending to within 0.3 cm. of the cortical surface. The sacs were covered by a smooth, glistening, greyish-white lining and contained multiple small, oval, brownish-grey calculi, the largest of which measured less than 1 cm. in diameter.

The right kidney was smaller, 14 x 4 x 0.8 cm., and weighed 50 g. (empty). Its capsule stripped with some difficulty, revealing a slightly granular, brownish-red cortical surface containing small retention cysts. On section, it was moderately hydronephrotic with multiple small locules extending deeply within the renal parenchyma. The renal tissue measured up to 0.4 cm. in thickness. There was no corticomedullary differentiation. The lining of the locules was smooth and glistening. The right ureter was patent and there was no obstruction to the flow of urine. The right renal veins were normal in course. The renal arteries were unremarkable. Both ureters, urinary bladder and prostate were normal.

Microscopic examination of the kidneys showed only a thin shell of distorted renal parenchyma. The changes were more marked in the left kidney. Scattered remaining glomeruli were shrunken and fibrotic with marked fibrotic thickening of Bowman's capsule. An occasional glomerulus was hypertrophied. In many areas the cortex was replaced by dense acellular fibrous tissue. In both kidneys, the medulla was replaced by dense hyaline and fibrous tissue infiltrated by lymphocytes. A few nests of tubules were left, some of which were

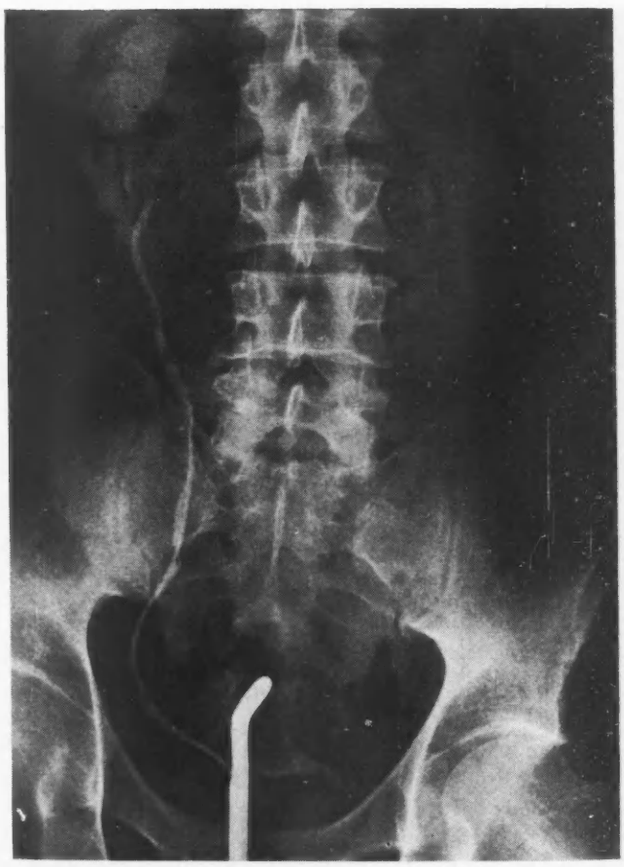

Fig. 1.—Patient G.H. Retrograde pyelogram shows grossly hydronephrotic right kidney.

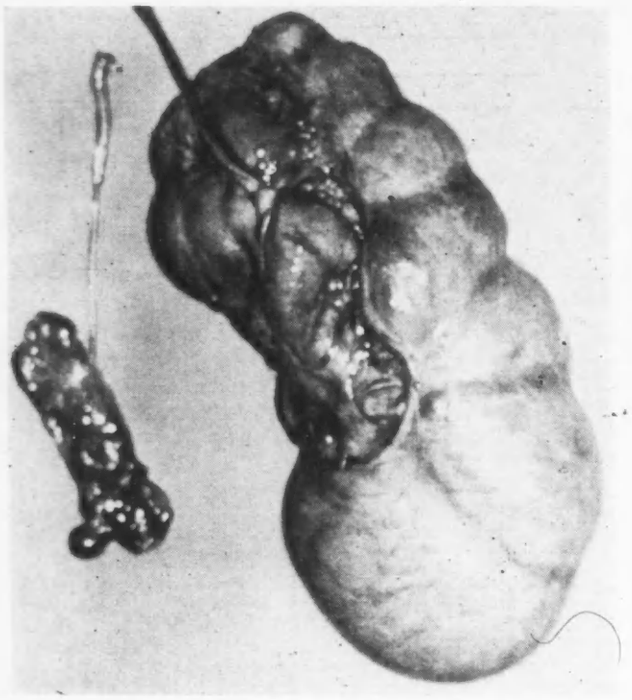

Fig. 2.—Patient G.H. Autopsy findings. The left kidney is markedly enlarged (34 x 9 x 17 cm.). An aberrant branch of the renal vein crosses and obstructs the ureteropelvic junction. The small right kidney was emptied of the fluid it contained.

Fig. 3.—Patient G.H. Section of the kidneys. Parenchyma of the left larger kidney is replaced by numerous sacs containing multiple small oval brownish calculi. The smaller right kidney shows a marked degree of pelvic and calyceal dilatation.

dilated and contained eosinophilic casts. The few remaining collecting tubules were distorted and degenerating. The hydronephrotic sacs were lined by dense fibrous tissue containing scattered fibroblasts. The small arteries and arterioles showed moderate sclerotic changes.

The spleen weighed 255 g. The capsule was irregularly wrinkled. On section, a firm splenic pulp was reddish-purple in colour. A small splenunculus was attached to the tail of the pancreas. On microscopic examination, the spleen was markedly congested. The lymphoid follicles were small and far apart, many without germinal centres. The small blood vessels showed moderately severe hyaline arteriosclerosis and arteriolar sclerosis with marked narrowing of the vessel lumens. The liver weighed 1660 g. Section and microscopic examinations showed moderate fatty degeneration and moderate congestion. The hematopoietic bone marrow was actively cellular and slightly hyperplastic. The erythroid forms predominated and numerous earlier forms were seen. Other series were normal.

There were slight to moderate arteriosclerotic changes in the cerebral, coronary, visceral and peripheral arteries. A small hamartoma was found in the right lung. The remaining organs were unremarkable.

In spite of the moderate uremia due to bilateral hydronephrosis, this patient continued to have excellent hemoglobin levels. Apart from splenomegaly, he showed a picture of erythrocytosis rather than polycythemia vera. Neither on physical examination nor in the history was there evidence of pulmonary or circulatory defect to suggest polycythemia secondary to chronic anoxia. It is inferred, therefore, that in this case the erythrocytosis could be related to bilateral renal disease in the same way that it is related to unilateral non-neoplastic renal disease in cases where erythrocytosis is abolished after nephrectomy. However, there is no absolute proof that he did not have coincidental polycythemia vera.

DISCUSSION

The establishment of a causal relationship between neoplastic or non-neoplastic disease and erythrocytosis is based chiefly on evidence that removal of the tumour or correction of the non-neoplastic disease results in remission or cure of the erythrocytosis.

In cases of erythrocytosis with renal disease not submitted to surgery such a causal association will be suggested though not proven if coincidental polycythemia rubra vera or erythrocytosis due to chronic anoxia can be ruled out. Because few cases of non-neoplastic renal disease in association with erythrocytosis have been reported, it is not yet clear which particular type of kidney lesion will prove to be responsible for the hematopoietic response.

The diagnosis of the polycythemic state may itself be difficult. It was pointed out by Lawrence[28] that hemoglobin levels, red blood cell counts and platelet counts should not be relied upon in making the diagnosis of polycythemia, and that elevation

of the red cell mass in relation to body weight and an increased iron turnover rate constitute definite evidence of the polycythemic state. It is suggested that relating the red cell mass to the lean body weight may make this parameter more precise.[21, 29] Thus, overweight individuals who would otherwise be excluded may fall within the polycythemic range.

It may be equally difficult to establish that erythrocytosis, in a case of tumour or of non-neoplastic disease not submitted to and corrected by surgery, is not coincidental polycythemia vera. Although lack of splenomegaly, leukocytosis and thrombocytosis is said to be rare in erythrocytosis of that type, according to Lawrence[28] splenomegaly may be absent in 44% of cases, leukocytosis (over 10,000 per c.mm.) in 25%, and thrombocytosis (over 300,000 per c.mm.) in 35%. Thus, certain cases of polycythemia vera may exhibit erythrocytosis alone, at least at some stage in their course.

On the other hand, review of the reported cases of erythrocytosis associated with tumour shows that splenomegaly, leukocytosis and thrombocytosis in these cases are not exceptional. In Forssell's review of a series of 25 cases of renal tumour associated with erythrocytosis,[11] splenomegaly was noted in five and platelet counts above 500,000 per c.mm. in three. In 10 cases reported by Damon *et al.*,[12] splenomegaly was noted in two and white blood cell counts above 10,000 per c.mm. in three. Similar findings have been reported in isolated cases of myofibroma[6] and hypernephroma[14] associated with erythrocytosis. In the present series of 13 cases of non-neoplastic renal disease and erythrocytosis (Table I), splenomegaly was observed in three, white blood cell counts above 10,000 per c.mm. in nine, and platelet counts above 500,000 per c.mm. in one. Furthermore, this polycythemia-vera-like picture may subside after removal of tumour, as does pure erythrocytosis. This is demonstrated by Forssell's Case 1 with an elevated platelet count and splenomegaly,[11] Lawrence's Case 2 with leukocytosis and thrombocytosis,[13] and possibly Drivsholm's case with splenomegaly.[14]

Other laboratory tests have not been helpful in differentiating polycythemia vera from erythrocytosis associated with tumours or non-neoplastic disease. The erythropoietic activity of the plasma has been found to be elevated in both varieties.[30-32] The iron turnover rate is increased in all types of polycythemia and the values overlap.[18, 21] The differential count of white blood cells stained for alkaline phosphatase was normal in two cases of polycythemia associated with tumours reported by Mitus, Mednicoff and Dameshek,[33] and with other secondary polycythemias, but was elevated in polycythemia vera. Whether this index will behave consistently in these two types of polycythemia remains to be seen.

For the time being, there is no clear-cut distinguishing feature of erythrocytosis associated with tumours and non-neoplastic disease; and in any given case not submitted to the test of surgery, a coincidental association of polycythemia vera cannot be ruled out absolutely. From a practical point of view the search for a tumour or renal disease appears to be indicated in cases of polycythemia not clearly due to pulmonary or circulatory disease.

The obscure relationship betwen polycythemia vera and erythrocytosis associated with neoplastic and non-neoplastic disease is further demonstrated by a case mentioned by Gurney in which erythrocytosis co-existing with polycystic kidney evolved after nephrectomy into unequivocal polycythemia vera,[22] and by Damon's case of a woman with uterine fibroids whose erythrocytosis subsided after hysterectomy and who six years later showed a picture of polycythemia vera.[16]

The overlapping clinical and laboratory features of polycythemia vera and erythrocytosis associated with tumours or non-neoplastic renal disease must also be considered in the light of recent advances in hematology. It is now generally accepted that erythropoiesis is regulated by a humoral factor, or factors, referred to as erythropoietin,[34-37] the production or activation of which appears to depend on the oxygen requirements of the tissues.[38, 39] Increased erythropoietin activity has been reported both in the plasma of patients with polycythemia vera and in those with secondary polycythemias.[30-32] Bethell and Linman[40] have shown that erythropoietin production does not depend on active bone marrow or lymphoid tissue in polycythemia vera. The plasma erythropoietin titre remains high in this condition, after the bone marrow has been effectively inhibited by a therapeutic dose of P^{32}. The source of the increased plasma erythropoietin in this myeloproliferative disorder has not been identified. On the other hand, a fall in plasma erythropoietin has been observed in cases where erythrocytosis subsided after nephrectomy or the removal of tumour.[21, 32] It is therefore possible that the difference between polycythemia vera and erythrocytosis secondary to tumours or renal disease may not be qualitative but rather a matter of the intensity and duration of the stimulus to which the bone marrow is subjected.

Cases of erythrocytosis associated with cystic kidneys or hydronephrosis are of added interest because of the experimental work of Jacobson and his associates,[41, 42] Naets,[43, 44] Osnes,[45-47] and Reissmann *et al.*,[48] indicating that plasma erythropoietic activity and erythropoiesis are dependent upon a humoral factor produced by the kidney. Although there is no general agreement on this point,[49, 50] it has been shown in animals that uremia *per se* is not responsible for anemia,[42, 43, 46, 48] as the bone marrow under those circumstances is still able to respond to erythropoietin. However, the ability of the bone marrow of the uremic animal to respond to stimuli, usually resulting in erythroid hyperactivity, and the presence of the erythropoietic principle in the plasma of these animals appears

to depend on the state and the amount of the residual renal tissue.[45, 46, 48]

These experimental observations have given a new impetus to the study of hematopoiesis in relation to renal function in clinical conditions.

Erythropoietin detected in low concentration under normal circumstances in the plasma of human subjects[51, 52] has been found in significantly higher concentration in the plasma and urine of patients with various anemias[40, 53-57] and in primary and secondary polycythemia.[30-32, 40] It is low or undetectable in anemias associated with malnutrition, chronic infection and, in particular, those of chronic renal insufficiency.[55, 58, 59]

The relationship between the amount of functional renal tissue as reflected by creatinine clearance, serum creatinine and blood urea on the one hand, and the hemoglobin levels on the other, was studied by Effersoe.[60] His observations, which paralleled very closely the experimental animal data of Osnes,[46] showed that normal hematopoiesis is preserved until some 70 to 80% of renal tissue has been destroyed. The present case of erythrocytosis associated with benign renal disease (in which the amount of the residual functional renal tissue must have been very small) and two similar cases referred to recently by Hewlett *et al.*[61] demonstrate that under certain circumstances uremia is compatible with hyperactive erythropoiesis.

The mechanism of production of the erythrocytosis associated with non-neoplastic renal disease is uncertain, but may differ from that in the case of tumour. In the latter, the assumption that the tumour tissue is elaborating the erythropoietic principle is in agreement with observations that neoplasms may reproduce various endocrine syndromes. Extracts of solid tissue or of cystic fluid from tumours associated with erythrocytosis have shown high erythropoietic activity in contradistinction to extracts from tumours not associated with erythrocytosis.[32, 61, 62]

On the other hand, the occurrence of erythrocytosis in cases of non-neoplastic renal disease raises the question whether the kidney may be stimulated by an intrinsic disease to produce the erythropoietic factor in excess. Experimental erythrocytosis in dogs has been produced by Van Lessen, Stefanini and Smith by means of unilateral partial ligation of the renal vein.[63] It was consequently suggested that involvement of the renal vein by tumour may explain the occurrence of erythrocytosis in some cases of hypernephroma. Although the experimental production of erythrocytosis is of great interest and may be pertinent to the mechanism of production of erythrocytosis in non-neoplastic renal disease, many obscurities concerning the renal hematopoietic factor hinder understanding of the role of the kidney in normal and abnormal hematopoiesis.

It is uncertain whether the kidney produces an active erythropoietic principle, a precursor of it, or a co-factor required for the activation of a principle produced at other sites.[42, 44, 47] At the present time, no information is available concerning the erythropoietic activity of the arterial and venous blood of various organs. In a case of erythrocytosis which subsided after removal of a hydronephrotic kidney, Jones *et al.* found high erythropoietic activity in the peripheral blood but not in the venous blood collected from the affected kidney.[21] Although various suggestions have been made,[44, 47, 48] the site of the production of the erythropoietic factor within the kidney is unknown.

It has recently been suggested that the vascular endothelium may be the site of the erythropoietin production.[64] The association of highly vascular tumours such as cerebellar hemangioblastomas or certain uterine fibromas with erythrocytosis could be explained on this basis as pointed out by Gurney.[22] On the other hand, the renal tissue, or a specialized part of it, equipped with the capacity to produce the erythropoietic renal principle may release it in excess when an extraordinarily strong stimulus is applied. This may also occur spontaneously when the renal tissue is undergoing neoplastic changes.

Further experimental work and clinical observation of appropriate cases may elucidate the role played by the kidney in the regulation of erythropoiesis.

SUMMARY

A case of "erythrocytosis" associated with bilateral hydronephrosis on a developmental basis has been added to the 11 such cases reported in the available literature.

In this case, erythrocytosis co-existed with longstanding uremia.

In all 12 cases, there was dilatation of the intrarenal excretory system and compression of renal parenchyma, and the incidence of developmental anomalies was high.

On the basis of clinical observation and tests, it is difficult to differentiate between erythrocytosis associated with tumours or non-neoplastic renal disease and polycythemia vera.

The emerging role of the kidney in erythropoiesis and possible mechanisms of production of erythrocytosis in cases of non-neoplastic and neoplastic renal disease are discussed.

We wish to thank Dr. D. J. Buchan and Dr. G. Chertkow for their permission to review and report this case; Dr. G. A. B. Cowan for providing the red cell mass, plasma and total blood volume determination data; Dr. J. W. Adams for permission to reproduce the autopsy report and photographs of the specimens; and Dr. T. A. Cunningham for valuable advice in the preparation of the manuscript.

ADDENDUM

Since this manuscript was completed and submitted for publication, four additional cases of erythrocytosis associated with benign renal disease have been brought to our attention. A case of bilateral unilocular renal cysts and erythrocytosis associated with splenomegaly has been reported by Cohen.[65] Of the three cases reported by Nixon *et al.*[66] two with unilateral cystic involvement showed a remission of erythrocytosis after the excision of

the cysts. In one of these cases in which the assay could be done, high erythropoietic activity was shown in the extract from the cyst wall and in the fluid which it contained. Their third patient had bilateral cystic renal disease, erythrocytosis and possibly splenomegaly. A case of a similar nature (Case 4) included in the recent paper by Ways *et al.*,[67] concerned chiefly with renal tumours and erythrocytosis, is less well documented.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

THE CANADIAN MEDICAL ASSOCIATION MEETING: 1911

The coming meeting of the Canadian Medical Association in Montreal bids fair to be one of the most largely attended and successful in the history of the Association. Coming as it does immediately after the functions connected with the McGill reunion, there is no doubt that a great many who attend the latter will remain for the Association meeting. The entertainment committee and the committee of arrangements have made special efforts to render the stay of visitors enjoyable.

On the evening of the first day, June 7, there is to be a smoker in the Victoria Rifles Armoury, and on the afternoon of the third day, a visit, by special train, to the Macdonald Agricultural College at Ste. Annes. One new feature, which it is hoped will prove particularly acceptable to the members of the Association, is the lunch offered to the Association by the Montreal members on Wednesday and Thursday in the new medical building, in which all the section meetings are to be held. It is anticipated that this will mean a great saving in time, and will serve to bring the members back punctually to the afternoon sessions, which begin at two o'clock. In the way of amusements, it may be mentioned that all the golf links around Montreal will be open to the Association members and the ladies who accompany them.

The provisional programme shows a very satisfactory list of papers, many of them of more than ordinary interest, while among the names of those who have been invited to address the Association are several which are very widely known. Sir James Barr, of Liverpool, is to give the address in medicine on Thursday evening in the Royal Victoria College, his subject being, "Preventive Medicine, the Medicine of the Future". Dr. Wm. J. Mayo, of Rochester, Min., is to give a paper on "Cholelithiasis: Natural History and Complications". It is sufficiently known that Dr. Mayo's experience in this subject is second to none. Dr. Primrose, of Toronto, is to deliver the address in surgery. In the ophthalmological section, Dr. Casey A. Wood, of Chicago, is to give a paper on "The Operative Treatment of Glaucoma", and Dr. J. P. McKernon, of New York, one on "Modern Methods of Diagnosis in Otological Practice". In the section of obstetrics and gynaecology, Dr. Howard Kelly, of Baltimore, and Dr. J. Clarence Webster, of Chicago, are to give papers. One of the interesting features of the meeting will be the demonstrations of newer methods in diagnosis. In the section of surgery, papers are to be read by Dr. J. T. Pilcher, and Dr. P. M. Pilcher, of Brooklyn, N.Y. Dr. J. Douglas Morgan, of Montreal, is to give a cinematographic demonstration of the normal movements of the heart.—Editorial, *Canadian Medical Association Journal*, 1: 543, June 1911.

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SUR UNE PROPRIETE HEMOLYTIQUE DU SERUM NORMAL*

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AU COURS de travaux récents sur les anticorps du sérum normal et sur les anticorps anormaux, nous avons utilisé, pour traiter les globules rouges, plusieurs enzymes. Les résultats d'ensemble seront rapportés dans une prochaine publication.[1] Dans le présent travail, nous nous en tiendrons aux résultats obtenus avec une protéase d'origine pancréatique, la *pan-protéase.*†

Lorsque l'on met en présence de leur propre sérum les globules rouges traités à la pan-protéase, on observe une importante hémolyse. Cette propriété se vérifie aussi lorsque l'on substitue aux globules rouges du sujet des globules rouges isogroupe traités de la même façon. Elle s'observe à 37° C et à 4° C, avec les différences et nuances que nous indiquerons ci-dessous.

MATÉRIEL ET MÉTHODES

Traitement des globules rouges (G.R.) à la pan-protéase (P.P.)

La solution de P.P. contient un mg. de P.P. par centimètre cube de tampon Sorensen à pH 7.7. On met en contact 0.2 cc. d'une purée de G.R. humains, préalablement lavés trois fois, avec un centimètre cube de la solution de P.P. pendant une heure, à 37° C. Les globules sont ensuite lavés deux fois en soluté salé physiologique et resuspendus à 2%.

Incubation des G.R. avec leur propre sérum

Dans un tube à hémolyse, on met un volume de la suspension de G.R. traités à la P.P. et un volume de la dilution sérique. Les tubes portés à 37° C sont inspectés au bout d'une heure. La lecture est macroscopique. On apprécie la couleur des surnageants et la disparition plus ou moins complète du culot globulaire.

L'étude a été faite chez 235 humains et chez 30 animaux. Les méthodes d'études du *complément* et de la *properdine* sont celles exposées par Soulier[2] et par Pillemer et ses collaborateurs.[3-6]

RÉSULTATS

Resultats obtenus à 37° C

Avec une dilution sérique de ½, on observe une hémolyse complète des G.R. chez 71% des sujets. Dans une plus faible proportion, soit chez 14% des sujets, l'hémolyse, bien que nette, s'étend de 50% à 10%, à la dilution sérique ½. Enfin, 16% des sujets testés ne présentent aucune hémolyse ou de faibles traces. Quant à l'intensité de l'hémolyse, quel que soit son titre initial, elle décroît régulièrement d'une dilution à l'autre (fig. 1).

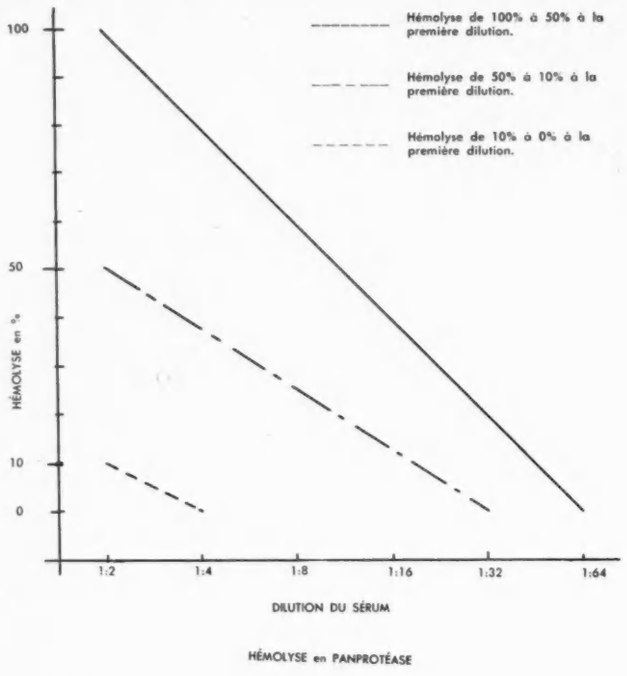

Fig. 1

Résultats obtenus à 4° C

Ils sont généralement parallèles à ceux obtenus à 37° C. On peut cependant noter des discordances. Ainsi, le sujet 38 hémolyse fortement à 37° C alors qu'on ne note aucune hémolyse à 4° C. L'inverse s'observe. Ainsi, les sujets 43, 44, 112 et 213 hémolysent leurs globules rouges à 4° C alors qu'on n'observe aucune hémolyse à 37° C.

La propriété hémolytique selon l'âge

Il n'y a pas de pouvoir hémolytique, en globules auto ou iso-groupe, chez le nouveau-né. Le sang du cordon en est dépourvu. Le pouvoir est faible ou absent chez le nourrisson et ne fait son apparition que vers le troisième mois. Il se manifeste d'abord à 2° C et plus tard à 37° C (10 mois).

L'hémolyse en pan-protéase chez les animaux

Le cobaye ne possède pas le pouvoir hémolytique à 37° C. Le lapin, par contre, hémolyse fortement ses G.R. à cette température. A 2° C, le pouvoir est présent chez le lapin. Le mouton ne possède de pouvoir hémolytique ni à 37° C ni à 2° C.

Rapports entre groupes sanguins et pouvoir hémolytique

Les sujets testés appartenaient à toutes les variétés possibles de groupes dans le système ABO et dans le système Rh.

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Travail subventionné par le Ministère de la Santé.
†Pan-Protéase, Worthington Biochemicals, Freehold, N.J., U.S.A. Cette protéase lyophilisée titre 4000 unités chymotryptiques et 7000 unités tryptiques au milligramme.

L'agglutination réversible à 37° C

Si on observe attentivement les tubes dans les premières minutes de contact, on voit parfois une fine agglutination se produire. Elle est spontanément réversible en quelques minutes. Elle se note particulièrement chez les sujets à faible pouvoir hémolytique. Soulignons que cette agglutination passagère ne se voit que rarement, qu'elle disparaît toujours spontanément et que le chauffage à 56° C, pendant 30 minutes, la fait disparaître totalement.

L'agglutination à 2° C

Si on chauffe le sérum à 56° C, pendant 30 minutes et qu'on le mette en présence de G.R. traités à la P.P. à 2° C, on observe une nette agglutination. Le titre en globules auto et en globules iso varie de 1/16 à 1/128 chez les sujets en santé, le titre de 1/64 étant le plus fréquemment trouvé.

TABLEAU I.

AUTO-AGGLUTINATION *à 2° centigrade—Comparaison des titres obtenus en globules non-traités avec les titres obtenus en globules traités à la pan-protéase ou à la trypsine.*

Numéro	*Complets*	*G.R. traités à la P.P.*	*G.R. traités à la trypsine*
98-A	1/2	1/128	
135	1/32	1/64	
136	1/16	1/32	
137	1/32	1/64	
156	1/4	1/64	
157	0	1/128	
158	0	1/128	
159	0	1/128	
160	1/4	1/64	
161	0	1/32	
162	1/8	1/128	
163	0	1/32	
164	1/4	1/64	
173	1/32	1/128	
177	1/8	1/32	
209		1/128	1/128
211		1/64	1/256
214	1/8	1/64	1/256
215	0	1/16	1/32
216	1/8	1/64	1/128
217	0	1/64	1/128
218	1/2	1/64	1/256
219	1/2	1/32	1/128
220	0	1/32	
218	0	1/32	

Nous avons, dans le tableau I, mis en parallèle les titres obtenus avec un même sérum, pour les anticorps complets froids, les agglutinines en globules pan-protéasés et les agglutinines en globules trypsinisés. On peut voir que le titre en pan-protéase et en trypsine est beaucoup plus élevé que le titre des complets froids, qu'il ne semble pas y avoir corrélation nette entre les complets froids et les agglutinines décelées sur les globules traités aux enzymes, comme en font foi les numéros 157, 215 et 217. Ces sujets ne présentent pas d'auto-agglutinine froide complète alors que le titre en enzymes est net. On peut noter aussi que le titre en trypsine est généralement plus élevé que le titre en pan-protéase.

L'hémolysine dans les sérums contenant un anticorps irrégulier

La présence d'un anti-D dans le sérum n'altère en rien le pouvoir hémolytique de ce sérum sur les globules auto ou iso compatibles, traités à la P.P. (des tests furent faits sur 121 anti-D différents). Les G.R. traités à la P.P., lorsqu'ils sont mis en présence d'un sérum contenant un anticorps chaud irrégulier, sont agglutinés par un tel sérum, en suspension saline. Il faut préalablement *chauffer le sérum.* Le chauffage fait disparaître l'hémolysine physiologique tandis qu'il n'altère en rien l'anticorps irrégulier, que ce soit un iso-anticorps (v.g. anti-D) ou un auto-anticorps. Nous utilisons cet enzyme dans la recherche des anticorps chauds irréguliers.

Rapport entre le pouvoir hémolytique en P.P. et le complément

Le chauffage du sérum à 56° C lui fait perdre, en même temps que C'1 et C'2, son pouvoir hémolytique sur G.R. traités à la P.P. L'addition de streptokinase qui détruit C'1 et C'2 fait disparaître le pouvoir hémolytique. La trypsinisation du sérum produit le même résultat. Dans le sang prélevé sur les anticoagulants tels que citrate de soude, oxalate de soude et séquestrène, le plasma ne possède pas de pouvoir hémolytique. L'addition d'ammoniaque au sérum lui fait perdre la fraction C'4 et en même temps son pouvoir hémolytique. Le sérum débarrassé de C'3 et de properdine par traitement au zymozan à 37° C n'est plus hémolytique. La chlorure de thiamine est aussi inhibiteur de la réaction.

Dosage comparatif du complément et du pouvoir hémolytique en P.P.

Les expériences précédentes ont bien démontré que le complément et ses fractions sont essentiels à la réaction d'hémolyse en P.P. La question se posait donc, à savoir si la substance responsable de cette hémolyse est le complément lui-même. Il semble bien, comme on peut le voir par le tableau II, qu'il n'en est rien. Si le dosage du

TABLEAU II.—HÉMOLYSE EN PAN-PROTÉASE—RAPPORTS AVEC LE COMPLÉMENT

Sujet	*Hémolyse en P.P.*	*Taux en complément par rapport au taux normal*	*Taux de C'3 (par rapport au taux normal)*
184	Nulle (0%)	49/45 unités	
186	Normale (100%)	45/45 unités	
187	Nulle (0%)	40/45 unités	
188	Normale (100%)	46/45 unités	
222	Normale (100%)	36/44 unités	
223	Moyenne (50%)	44/44 unités	80/80 unités
224	Nulle (0%)	59/44 unités	98/80 unités
226	Nulle (0%)	25/52 unités	88/97 unités
227	Normale (100%)	54/52 unités	116/97 unités
44H	Nulle (0%)	53/52 unités	97/97 unités
229	Nulle (0%)	26/52 unités	50/97 unités

N.B.—Ce tableau résume les résultats obtenus chez 34 sujets. Nous n'avons inscrit que 11 cas, parmi les plus représentatifs.

complément montre que celui-ci est essentiel à la réaction d'hémolyse en P.P., on peut voir, par contre, que des sujets possédant du complément en quantité normale n'ont pas (ou très peu) d'hémolyse en P.P. (Cas 184, 224, 187, 226, 44H). On peut dire la même chose du dosage de C'3.

Rapports avec la properdine

En utilisant le dosage qualitatif de la properdine, on constate les mêmes discordances qu'à propos du complément. (Tableau III). Le cas 269 a un faible pouvoir hémolytique en pan-protéase alors que la properdine semble présente en quantité normale. Mêmes observations pour les cas 289 et 290.

TABLEAU III.—HÉMOLYSE EN PAN-PROTÉASE—RAPPORT AVEC LA PROPERDINE (POUVOIR HÉMOLYTIQUE SUR G.R. TANNÉS)

Sujet	*Hémolyse en pan-protéase*	*Hémolyse en G.R. tannés*
269	10%	100%
270	100%	100%
90B (sérum vieux de 2 jours)	0%	0%
296	10%	50%
25K	0%	50%
273	10%	100%
286	100%	100%
287	100%	100%
288	100%	100%
289	0%	100%
290	0%	100%
291	100%	100%
298	100%	100%
299	100%	100%

Le RP, c'est-à-dire le sérum débarrassé de sa properdine par absorption sur zymozan à 17° C, a perdu son pouvoir hémolytique en P.P.

Il semble que l'on puisse dire que la properdine n'est pas elle-même uniquement responsable de la réaction. D'ailleurs, nous avons confirmé ces premiers résultats par les dosages quantitatifs de la properdine et du pouvoir hémolytique en P.P. sur les mêmes sérums. Les résultats obtenus confirment ceux qu'a donnés la méthode qualitative. Par exemple: le sujet 235 n'a pas de pouvoir hémolytique contre les G.R. traités à la P.P. alors que son taux de properdine est normal, soit de 4 à 8 unités. Les sujets qui n'ont pas de properdine n'ont pas non plus de pouvoir hémolytique. Ainsi, la properdine, comme le complément, est essentielle à la réaction mais n'en est pas uniquement responsable. Un seul résultat discordant a été obtenu. Il s'agissait d'une patiente souffrant de maladie de Hodgkin, qui avait une hémolyse normale alors qu'elle était dépourvue de properdine.

Recherche d'une action hémolytique de la trypsine et de la chymotrypsine

Les globules rouges traités par l'un ou l'autre de ces deux enzymes qui constituent la pan-protéase, ne sont pas hémolysés par le sérum normal.

RÉSUMÉ ET DISCUSSION

Le sérum normal possède la propriété d'hémolyser les G.R. (auto ou iso) traités par un complexe enzymatique, la pan-protéase. Ce pouvoir a été constaté à des degrés divers, chez 85% des 235 sujets testés. Il se manifeste à 37° C et à 2° C. Entre autres caractéristiques, le complément et la properdine sont nécessaires à la mise en évidence de cette hémolysine particulière. Cette hémolysine n'est cependant, ni le complément, ni une de ses fractions, ni la properdine.

Malgré des travaux considérables, on ne sait que peu de choses des réactions qui conduisent à la désintégration du globule rouge rendu au terme de son existence. Il n'est pas interdit de penser qu'une propriété sérique, assimilable à l'hémolyse ici décrite, ne "reconnaisse" les globules vieillis et ne conduise à leur désintégration dans le système réticulo-endothélial. De toutes façons, l'étude des propriétés hémolytiques du sérum normal mérite d'être poursuivie, même à partir de systèmes artificiels tel que celui que nous avons décrit dans le présent travail.

SUMMARY

Normal serum hemolyzes autologous or isologous red blood cells treated with an enzymatic complex known as pan-protease. This property was demonstrated at different degrees of activity in 85% of 235 patients tested. It operates at 37° C. and at 2° C. This hemolysin will work only in the presence of complement and properdine, yet it is neither complement or any of its components, nor properdine.

In spite of considerable work, very little is known of the process through which red cells disintegrate at the end of their life-span. It appears reasonable to suggest that a serological fraction similar to the hemolysin referred to above would identify old corpuscles and shunt them out of the circulation over to the reticuloendothelial system for their destruction. Be that as it may, hemolytic properties of normal serum deserve further study even through the use of such artificial systems as the one described in this paper. M.R.D.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

OTTAWA MEDICAL SOCIETY

The last meeting of the season of the Ottawa Medical Society took place at St. Luke's Hospital, April 14, 1911. Dr. A. T. Shillington reported a case of partial gastrectomy for cancer of the pylorus. Dr. Shillington considers in these cases that it is best to do a gastroenterostomy first, and in a few weeks, when the patient has gained some strength, to perform the gastrectomy. The operation was successful, and although six months have elapsed the patient is well and strong.

Dr. G. P. Howlett gave a report of one hundred and eighty-six cases of typhoid fever treated in the Emergency Hospital in Ottawa during the recent epidemic. Dr. Howlett was in charge of the hospital. The death rate was eight per cent. There were three cases of perforation, two of which were operated upon. Only one survived.—*Canadian Medical Association Journal*, 1: 587, June 1911.

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SPECIAL ARTICLE

BLOOD BANKING
II. ORGANIZATION AND PERSONNEL*

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WHILE great emphasis is rightly laid upon the techniques of cross-matching, the majority of hemolytic transfusion reactions are due to errors in patient-blood identification. In this way the ABO system remains the most common cause of such reactions. The clerical and administrative procedures in the blood bank and other areas such as emergency departments, operating rooms and the rest of the hospital must be designed to guard against such errors. All personnel handling blood must follow through repeated checks of patient, cross-match specimen and bottle identification. This paper will outline some of these aspects of blood banking that we have found helpful and review our experience with the training of blood bank personnel. As with all administrative systems, the descriptions that follow make the procedures sound much more complex than they are in practice.

Requisitions

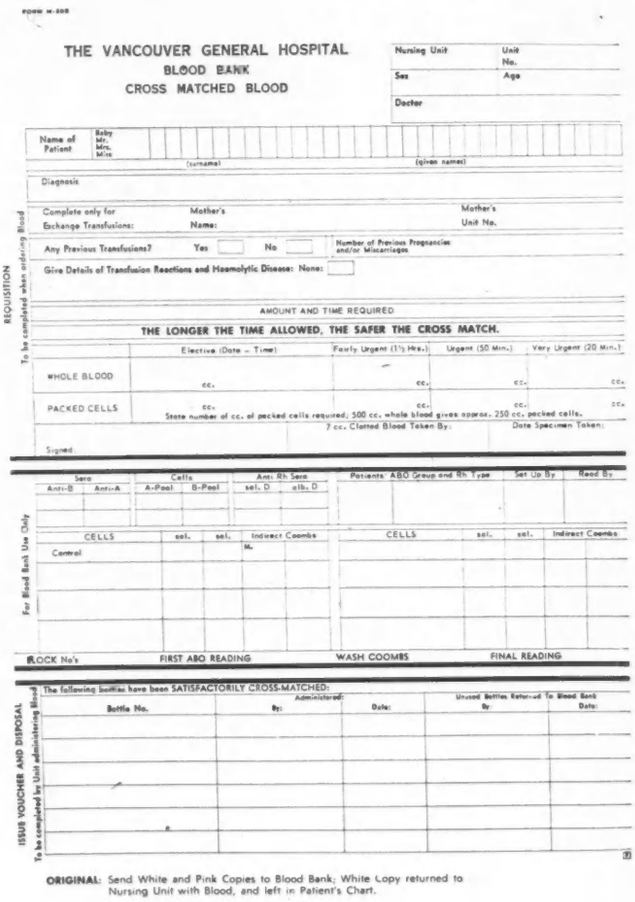
Identification errors frequently occur when information is copied from one sheet to another. This danger is avoided by having the request for blood, patient identification, cross-match work sheet and disposal of each bottle placed on a single requisition. The requisition should have two carbon copies, one of which may be retained on the ward and used later to obtain the cross-matched blood. Such a requisition is illustrated in Fig. 1.

The upper portion of the form identifies the patient and indicates the amount of blood required and the urgency of the request. Where any doubt exists as to the patient's identification, e.g. in the case of unconscious patients on admission, the hospital should have a method of identification available such as a numbered tag to be conveniently attached to the patient.

The middle section of the requisition is for the use of the blood bank and records the results of the grouping and cross-matching.

The lower section is completed by the individual starting the infusion of each bottle of blood or by the individual who returns the unused blood to the blood bank.

The cross-match form is completed in triplicate, i.e. an original (white) and two carbon copies


THE VANCOUVER GENERAL HOSPITAL
BLOOD BANK
CROSS MATCHED BLOOD

Nursing Unit | Unit No. | Sex | Age | Doctor

Name of Patient | Diagnosis | Complete only for Exchange Transfusions: Mother's Name: | Mother's Unit No. | Any Previous Transfusions? Yes No | Number of Previous Pregnancies and/or Miscarriages | Give Details of Transfusion Reactions and Haemolytic Disease: None:

REQUISITION — To be completed when ordering Blood

AMOUNT AND TIME REQUIRED
THE LONGER THE TIME ALLOWED, THE SAFER THE CROSS MATCH.

	Elective (Date – Time)	Fairly Urgent (1½ Hrs.)	Urgent (50 Min.)	Very Urgent (20 Min.)
WHOLE BLOOD	cc.	cc.	cc.	cc.
PACKED CELLS	cc.	cc.	cc.	cc.

State number of cc. of packed cells required; 500 cc. whole blood gives approx. 250 cc. packed cells.
7 cc. Clotted Blood Taken By: Date Specimen Taken:
Signed

For Blood Bank Use Only

Sera: Anti-B	Anti-A	Cells: A-Pool	B-Pool	Anti-Rh Sera: sol. D	alb. D	Patients' ABO Group and Rh Type	Set Up By	Read By

CELLS	sol.	sol.	Indirect Coombs M.	CELLS	sol.	sol.	Indirect Coombs
Control							

BLOCK No's | FIRST ABO READING | WASH COOMBS | FINAL READING

ISSUE VOUCHER AND DISPOSAL — To be completed by Unit administering Blood

The following bottles have been SATISFACTORILY CROSS-MATCHED:

Bottle No.	Administered: By:	Date:	Unused Bottles Returned To Blood Bank By:	Date:

ORIGINAL: Send White and Pink Copies to Blood Bank; White Copy returned to Nursing Unit with Blood, and left in Patient's Chart.

Fig. 1

(pink and yellow). The original (white) and the first carbon copy (pink) are sent to the blood bank as a request for blood and are used by the blood bank for cross-matching. The second carbon copy (yellow) has two uses: when the requisition is made out on the ward it indicates that blood has been ordered; later, when the ward is notified by the blood bank that the blood is ready, this copy becomes a demand slip which is used to obtain the blood from the blood bank. The original copy (white) is returned to the ward with the blood and becomes part of the patient's chart. The first carbon copy (pink) becomes the blood bank copy from which a card is typed to form a permanent file in the blood bank as described below.

The specimen taken from the patient for cross-matching requires a label with identifying information similar to that on the requisition form, i.e. the patient's name, unit number, nursing unit, physician and date. The checking of identification on the requisition and cross-match specimen is of prime importance and is carried out both at the beginning and at the end of the cross-match procedure, each check requiring a tick mark on the top of the requisition. The requisition is time-stamped on arrival of the cross-match specimen at the blood

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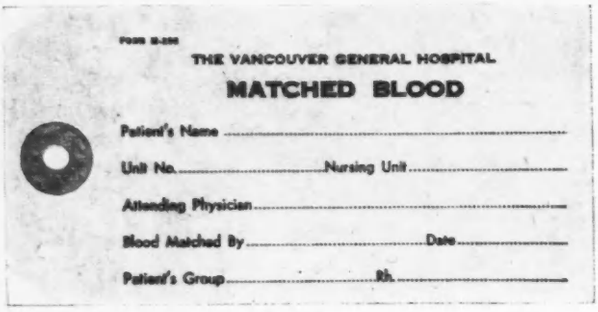
FORM B-255
THE VANCOUVER GENERAL HOSPITAL
MATCHED BLOOD
Patient's Name
Unit No. Nursing Unit
Attending Physician
Blood Matched By Date
Patient's Group Rh

Fig. 2

bank and is also time-stamped when the cross-match is finished. Each cross-match bottle is tagged (see Fig. 2) identifying the patient. On the reverse side of the tag is placed the serial number of each bottle.

Thus when the blood is being released from the blood bank the identification on the second carbon copy (yellow) brought from the patient's chart is checked against the original requisition (white), which in turn is checked against the serial number of each bottle and the complete information on each tag. The information concerning each bottle and patient is then entered in a Red Cross Whole Blood Record Book and later the disposition of the blood is noted.

Blood is currently issued from the blood bank to the ward without a return time limit. Used bottles are held on the ward for 24 hours and are then returned to the blood bank. If the bottle is not returned in three days, the ward is telephoned requesting immediate return of the blood. Ideally, blood issued and not used immediately would be promptly returned to the blood bank where it would be cancelled automatically at the end of three days, unless its cancellation was ordered immediately on return.

A separate requisition somewhat similar to that illustrated in Fig. 1 is used for obtaining unmatched blood, plasma, albumin, gamma globulin and fibrinogen. Unmatched blood and plasma each have distinguishing identity tags.

Plasma and packed cells have, in addition to a tag, a small bright green sticker indicating a six-hour expiry time.

Because the hospital buildings cover four blocks, a small reserve of group O Rh positive and Rh negative anti-A_1B hemolysin-free blood is kept in the case room and emergency department for immediate use.

A separate form is used to report transfusion reactions, and an investigation as previously outlined is carried out immediately. The initial results are telephoned to the ward and a written report is sent later.

Records

A permanent file in the blood bank provides a further measure of safety for the patient. From the pink copy of the requisition which is retained in the blood bank, all pertinent information is transferred to a standard 5 x 8 inch file card. These cards are coloured to match the Red Cross labels identifying the ABO group and are filed alphabetically. In order to guard against errors being made in typing the cards, the information on the requisition and cards is then checked by two people and at a later date the disposition of the blood is noted. Records of unmatched blood and blood products are typed on an orange file card.

In order to minimize the number of active cards, a separate file of deceased patients, whose names are obtained from the daily hospital record, has been in use for three years and accounts for 10% of the total number of cards.

Transfusion problem cases such as those presented by cross-matching difficulties, transfusion reactions and exchange transfusions are maintained in a separate file. The 5 x 8 inch file cards are specially marked in such instances to indicate that there is a special file on this patient.

In addition a log book is maintained in which each shift of technicians notes the unusual occurrences during their shift. This provides an immediate appraisal of the current blood bank problems and has proved to be of unexpected value.

Transfusion Therapists

Since 1949 almost all of the intravenous solutions and transfusions given in the Vancouver General Hospital, exclusive of those used in the operating room and emergency areas, have been administered by specially trained registered nurses now referred to as "transfusion therapists". In addition to these duties such personnel take almost all specimens for cross-matching and issue the major portion of the blood from the blood bank. During these years they have made no errors in starting 34,700 blood transfusions. There have been three errors involved in the administration of 220,400 intravenous infusions, none of which were serious, and two errors in taking 60,000 cross-match specimens. Both of the latter errors were discovered at some point in the later checking procedures.

It should be pointed out that transfusion therapists do not start the following intravenous solutions: (a) distilled water; (b) glucose in concentrations greater than 10%; (c) potassium in concentrations greater than 40 mEq./l.; and (d) noradrenaline, Neosynephrine, adrenaline, Mephyton, nitrogen mustard and other radiomimetic drugs.

The advent of a safe, simple intravenous polyethylene catheter will shortly result in modification of the foregoing regulations.

New therapists spend four weeks in training with the intravenous team before they take sole responsibility on a shift. Special emphasis is placed on patient identification and the checking procedures already outlined. At the end of three months they have encountered most of the problems they are likely to meet.

We believe that transfusion therapists are an important adjunct to the services of a hospital and that their skill, experience and care add greatly to the quality and safety of the blood bank service. Having their headquarters in the blood bank results in close liaison between the transfusion therapists and the blood bank technicians as well as with the ward nursing staff. At the present time nine full-time therapists and one half-time therapist provide this service for the 1500 beds of the Vancouver General Hospital from 7 a.m. to 11.30 p.m., seven days a week.

When a blood transfusion is already running, additional blood is added by ward personnel. Two ward nurses must check the patient-blood identification before starting the additional bottle.

Blood Bank Technicians

In Vancouver there has been a shortage of registered technicians with blood bank experience. The average technician on completion of training has been unable to cope with the routine work of a large hospital blood bank. Few laboratory personnel require a higher degree of devotion and assume more responsibility than do blood bank technicians. Blood banking is unique amongst laboratory procedures in that there is no clinical check on the work done by the technician. This imposes a great deal of responsibility on blood bank technicians that is not felt by technicians in other departments. It is the authors' opinion that further time should be devoted to blood banking procedures during the training period for registered technicians.

While smaller hospitals may have to use an "on call" system, larger institutions should have personnel on duty in the blood bank during the entire 24-hour period. Since many of the most difficult problems arise during the evening or night, a high standard must constantly be maintained among the personnel so employed. This type of coverage demands a great deal of shift work, and a willingness to accept this is an important feature in determining the selection of personnel for this work.

Because of the difficulty in obtaining technicians to do blood banking, it was decided two years ago to engage personnel with no previous laboratory experience and train them during a three-month period of lectures and bench work. This group was chosen from the staffs of other departments of the hospital following personal interviews. Emphasis was laid on willingness to do shift work and to accept responsibility, and an effort was made to pick those with a mature outlook. In particular an attempt was made to select individuals with intellectual ability but who, for lack of opportunity, had not attained the standard of education of which they were capable. The average level of education among those selected was close to junior matriculation (grade 12).

The curriculum of training was as follows. During the initial two months, 24 hours of lectures were devoted to general physiology, anatomy and pathology with emphasis on hematology. A further 24 hours of lectures were devoted to instructions regarding general blood banking. In addition some 20 hours of technical lectures were fitted in the appropriate places in this curriculum. The remainder of the time in the first two months was devoted to directed technical experience. During the third month the candidates were indoctrinated into the routine of the blood bank. The necessity of having an experienced head technician for such a training course can hardly be over-emphasized.

During the three-month training period a reasonable stipend was provided. This group has provided reliable, interested technicians who, although somewhat lacking in knowledge of general laboratory procedures, have a superior knowledge and skill in their own particular field which far offsets any lack of knowledge in other aspects of laboratory medicine. Their remuneration is slightly less than that received by a registered technician.

Resident Training

The blood bank in common with other aspects of clinical pathology is having to deal with a constantly increasing work load. Because of the current training requirements the average pathologist on completion of his training is, in the authors' opinion, inadequately trained in clinical pathology. This is frequently evident in regard to his inability to deal with problems arising in the blood bank. We are of the opinion that there should be further stress on the clinical aspects of pathology during the four years of training in general pathology. This would provide the general hospital pathologist who faces these and other clinical pathology problems with a more realistic and balanced background.

The establishment of an additional approved separate training program to cover only the branches of clinical pathology should be considered. Then a hospital with an establishment of two pathologists could employ one general pathologist and one clinical pathologist.

In our current training program each pathology resident spends one month acquiring practical experience in blood banking procedures. Then, during his three- to five-month period of training in general hematology, he assumes some supervisory responsibility for the daily problems of the blood bank. This program is currently under review.

SUMMARY

The organization and training of blood bank personnel has been reviewed. The importance of a requisition that has space for patient identification, cross-match work sheet and disposal of every bottle of blood, as well as a carbon copy for obtaining the correct blood, is stressed. A permanent file record on standard 5 x 8 inch cards has proved to be of great help.

Eleven years' experience with a program in which intravenous infusions and blood transfusions have been started by specially trained nurses who have also been

responsible for taking cross-match specimens has established clearly their great value in contributing to this aspect of patient care.

Two years of experience with blood bank technicians who, without previous laboratory experience, were given a three-month course of training has proved most satisfactory. Intellectual ability, rather than the standard of education attained, a pleasing personality and willingness to do shift work and accept responsibility were the important features in choosing these individuals.

A plea is made for an increase in the amount of clinical pathology required during the training of pathologists.

The authors would like to thank Dr. H. K. Fidler, Director of Laboratories, for his encouragement and helpful criticism.

VIEWPOINTS

BASIC ISSUES IN HOSPITAL AND MEDICAL CARE INSURANCE*

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AT THE end of this century it may well be said that our two main accomplishments in the field of health have been first, the fabulous progress in science and the impact of this on patterns of disease and life expectancy, and second, the distribution of these benefits of scientific advance to entire populations.

For the purpose of discussion, let me argue that the biggest problems relating to hospital and medical care insurance are not administrative and financial. They are, I submit, in the realms of (a) the art and technology of medicine and (b) the characteristics of our culture and the social forces determining them. In other words, the main questions are not how to devise and pay for insurance to cover expenses of stay in hospital, of illness at home and of visits to the doctor. More difficult by far are these questions: What are the health expectations of the Canadian people? How are these likely to change in the foreseeable future? Are prevailing assumptions sound? For example, in the various segments of our society what are the gaps between health *expectations* and health *needs*? By what measures (persuasive, administrative or compulsory) may these gaps in understanding be narrowed? Considering our Canadian health needs, what should be our long-term objectives, and considering our expectations and our resources, what would be a good health program? Undoubtedly it would include some form of hospital and medical care insurance. What are the relative advantages and hazards of insurance proposals currently before us? Along with control of the financial hazard of illness, are there other objectives to include in a good health program? Reliable answers to such questions can scarcely be expected without seeking a view of all elements in this complicated situation and in their best historical perspective. The movements leading to these accomplishments in science and to the better distribution of health benefits are still on the march and their somewhat dislocating impact on our settled ways of doing things will be even greater in the future. The task of assimilating the consequences of technological advance and of the movement towards the welfare state may shake our society to its foundations. Since these movements now are global it is clear that Canadian policy, even in health matters, will be affected by developments outside our borders. By the same token we cannot help but influence, for better or for worse, the evolution of health norms and facilities elsewhere in the society of nations. It is important, therefore, to be sure that the steps we take are on the firm ground of a sure science, in the direction of general human betterment and with a clear view of hazards, as well as rewards, lying ahead. The remarks that follow are to point up issues for discussion on a wide front. Their provocative purpose, as well as the need of brevity, will result sometimes in dogmatic, undocumented assertions. The opinions expressed are personal.

If the breakneck rate of progress in medical science is uninterrupted, it is staggering to think of how it will alter present patterns of disease. Expectations of increased longevity and possible freedom from physical misery may alter radically the routines of industry, family life and health services as we know them. Just as we have seen virtual miracles in the control of infection, in the surgery of the heart and brain and in the correction of a wide variety of chemical disorders, so we may expect control of cancer, the transplantation of organs and a delay in facing the ravages of old age. The benefits will be exciting but they will be at a cost. For one thing, we can be quite sure that new problems will arise. New treatments and diagnostic methods beget new hazards, just as seen in radiation procedures and in the development of resistance by bacteria to antibiotic drugs. We shall probably be travelling faster, with more work for

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the surgeon in the accident ward. Unless present trends change, we shall be eating more, exercising less and living under still greater nervous tension. The stress diseases will increase and unless our society is somehow stabilized we may have more psychiatric invalids despite vastly improved treatment. All of this means more elaborate equipment and organization in hospitals; more skills and knowledge to be mastered by physicians, nurses, technicians and therapists; a greater division of labour among the treatment team and, of course, a progressively greater financial burden.

The effect of all this upon people is already of concern. With more minute scrutiny of the various parts of a patient, the more danger there is of forgetting about him as a person—a human entity with dependencies upon job, family, community and social heritage. The doctor too is having a disruptive experience. One set of forces drives him farther from his colleagues by the division of labour, stimulating ever new specialties; on the other hand, the need of co-ordinated effort drives him into team work for which he may not be prepared. Let me counteract this note of gloom by stating that there are corrective measures in medical and nursing education and that there is growing awareness of these problems in hospitals and professional societies. Later, they will all come into focus when we speculate on the kind of physician most needed in this era of rapid technological change.

The second movement, that of ensuring equality of opportunity and a minimal standard of living for all in the group, is exceedingly complex; yet most people see it in the narrow context of their own niche in society and their family or class culture; too often they are unaware of historical determinants. Only a few of the implications for the field of health care will be dealt with. Perhaps the main thing to recognize is that the movement towards security in health is overwhelming; it is global and rightly or not it is identified with many of the good causes in history. Not to face this realistically, in my opinion, is to emulate the ostrich. Then there is confusion in the realm of ethics. We are emerging from an era when measures to gain health have been looked on as commodities to be purchased. As such they are more readily available to those rewarded by a sufficiency of this world's goods, supposedly by virtue of ingenuity, enterprise and hard work. The prevailing mood now is to recognize that accidents and disease strike both the righteous and the slothful, and that somehow people must organize collectively to be sure that the means of coping with the main hazards to health are available to all. In other words, within our lifetime a modicum of opportunity for good health has become a right rather than a limited privilege. Although it may be proved eventually that health programs are justified on grounds of increasing the economic productivity of society (just as rehabilitation of veterans paid for itself in terms of increased earnings), nevertheless for many Canadians the right to health is an ethical stand. It rests on the premise in our cultural heritage that man is morally bound to relieve suffering in his neighbour.

I have laboured this elementary point because of the frequency with which some otherwise mature Canadians oppose certain medical care provisions on the ground that they destroy initiative, inhibit responsibility and weaken the nation's moral fibre. This kind of argument seems hollow in the face of the preventable death of a mother or a child blighted for life because medical care was sought too late. I make the assumption that thinking people have accepted a concept of social responsibility for the promotion and preservation of health. This entails more than ensuring ability to pay for hospital and medical bills. It means a positive approach to the problem of integrating a cluster of services, including health education, to produce a physically robust and mentally healthy people. In this kind of quest quality is of the essence and the objectives must be clear.

At the beginning I hinted that what people expect of health facilities may not be identical with what they really need. So often what we clamour for has to do with the mood of the times; health definitely has its fashions. What do Canadians expect and what do we really need? Some of our perfectly valid expectations are these: prompt response to our requests for help; sound advice when we are troubled, as well as help in keeping out of trouble; excellence in hospital care and enough beds to accommodate us; up-to-date professional services from doctors, nurses, pharmacists and the host of others in the modern health team; also, freedom from financial catastrophe when major illness strikes and, if possible, a painless method of paying for it all. We assume too that the community is on its toes in protecting us from epidemics and various environmental hazards.

These are all reasonable requirements to meet genuine health needs. We often expect other features, however, which are less valid. More and more we rely on the hospital for services which might better be rendered in the home, in the doctor's office or in the public health clinic. When in the hospital we expect our backs to be rubbed, our meals to be served at the bedside and the menu to resemble that of a good hotel. Moreover, we are guilty of misuse of highly trained health personnel. Too often the bed is still made by a graduate nurse, the needle is administered by the doctor, and for even simple surgery the most senior consultant in town is demanded. Many patients do a bad job of deciding themselves when to go to a specialist, and some families insist on all care being rendered by a whole platoon of specialists. In many regions the practice of "shopping around" is denying the possibilities of the best care. Every one of these features adds unnecessarily to the cost of these essential services.

In less tangible aspects we have become unrealistic too. The concept of access to good care for all has been extended to the idea of a birthright of freedom from all physical discomfort, from guilt and anxiety and even, one would think, sometimes from death itself. These distortions have a bearing on the load thrown on medical personnel; they point up also the importance of health education as one element in a good health plan.

It must be apparent that much of what we expect of health services has to do with the cultural characteristics of our society. These, of course, are shared by doctor and patient alike. As such too they are susceptible of objective survey and analysis. We are just on the verge of an era in which more accurate knowledge of our assumptions and biases and behaviour patterns will be available. These vary greatly across Canada according to differences in regional history, in ethnic origin, in predominant age group and in economic status. When contemplating major undertakings involving public acceptance of a program with so many facets we need much more precise data than we have. This calls for social science research on a vastly larger scale than at present. Each province should have its teams of social scientists at work in the university, in government and in the voluntary agency too.

Two other features of our health scene require mention before we consider other health needs and our objectives. One, a consequence of scientific advance, is the large role played by machinery in modern medicine. With a plethora of x-ray procedures and laboratory tests we have tended to assume that most human misery stems from disorders to be elucidated by these technical means. This places the emphasis in treatment on the plane of something to be corrected mechanically or chemically. The analogy is with the garage, whereas a good deal of the healing of our ills is dependent really on the methods of the schoolroom and the shrine. In our culture the laying on of hands has been replaced by the electrocardiogram, the operation and the dose of vitamin or hormone. When these are administered by a healer (doctor, nurse, pharmacist *et al.*) who is friendly, interested, reassuring and authoritative, then we feel better. We are just learning to separate the specific biological effects of these measures from their ritualistic role as vehicles for psychotherapy. The relative importance of these two elements in treatment of illness among Canadians today is unknown. Here again we have a big research job to do. The results would probably reduce the bill for tests and operations and drugs; it would increase it for the personal services of the physician, because he would spend more time listening and explaining. The results in the latter case, however, would be better in the long run.

The other feature is our cultural link with money. We measure success in life in terms of money and what it purchases. It is normal to try to strike bargains, even to get something for nothing. At the same time, many people act on the theory that the best things always cost more; the less expensive article or method is suspect. This has made it difficult to equate many items of medical diagnosis and treatment to a dollar value. If the patient has troubles which require listening and explaining by the doctor, it is very hard to equate the value of this to dollars. Even in the prepayment plans run by physicians this problem has not been solved satisfactorily; internists and psychiatrists, unless they operate laboratories or use additional technical treatment, seldom get remuneration in keeping with the job done. This whole subject is admittedly difficult to appraise. It is related of course to the matter of fee-for-service and what its effects are on both patient and doctor. Sooner or later we shall have to decide whether the doctor's job resembles most that of the consulting engineer, or that of the teacher and minister.

What kind of health care do we need? Bearing in mind the scientific advance lying ahead and the socio-economic factors touched on above, it seems logical to expect that the care must be rendered by a team. At the same time there will be more need than ever for the potential patient to be related to one member of the team in a clearly personal way; someone who will remember him, who will know his strengths and foibles and whose obligation without question is to foresee and forestall the breakdowns in health. This kind of doctor should be specially trained in the skills of diagnosis because, more than ever before, early treatment is crucial. He should know when and how to obtain for his patient the necessary attention of specialists and he should be familiar with the social resources of the community which are increasingly helpful. Above all, he must have ample time to talk with the patient, to get to know him as a person rather than as "a heart" or "a liver", and certainly not as a source of five or ten dollar bills!

Whether the term "general practitioner" is a suitable label, because of its connotation of personal coverage on nearly all fronts, is open to question. He could be called a "family physician" if he looks after most of the members of the family. In any case, his role is that of "personal physician" and perhaps this is a good name for him. More important is that we learn how best to train him. Then we must make sure he is established in circumstances that will facilitate his role; and finally we must do all possible to accord him the prestige and the reward in keeping with his great importance.

What kind of health program does Canada need? First, let us make sure that our medicine is as good as the best. This means much more than finely equipped hospitals and technically competent doctors. The whole structure would fall if we had second-rate halls of learning and did not do our share to advance the science on which modern medicine rests. This means more support for our

universities. Most medical schools are desperately short of space for research and for the most modern teaching methods. We need many more bursaries and postgraduate fellowships if we are to recruit and develop the teachers needed now and for expansion in the near future. Next, let us offer *comprehensive* health services. These include the public health facilities serving the nation, the provinces and the municipalities; the preventive measures handled by the doctor if he is given the time (and the assignment); diagnostic facilities, including special case-finding surveys for those disabilities for which we can do something; treatment resources for acute and long-term illness; and finally, a rehabilitation program that will salvage as many as possible for lives of greater usefulness.

Then we must make sure that our good health care is available to all. This calls for two kinds of action. One is an appropriate geographic distribution of the facilities; the other is removal of the economic barrier to their utilization by all. The *regional* organization of health facilities is essential. There is enough accumulated experience to remove it from the realm of foolhardy experimentation. In essence, it entails a suitable spreading out of various kinds of hospital, specialist services and health agencies into secondary and tertiary centres. Coordination of the regions need not thwart the development of considerable autonomy of action in each region. The benefits of self-determination are then joined to the great advantage of being able to study the relative merits of different approaches.

The removal of the economic barrier to adequate health care, it will be noted, is somewhat down my list of items for attention in a good health program. This is not to diminish its importance but to emphasize that the solution of the financial problem of the individual or family does not of itself ensure high-quality care. We are now in the realm of public controversy and all I shall do is state my own views, not all of which are held with equal conviction. I think there are advantages in a *contributory* plan. We all take more interest in a venture in which we have some obvious stake. At the same time it would be impossible to finance a comprehensive program by premiums alone; they would be too heavy for a portion of the population. The balance of support, i.e. beyond premiums, would come from general revenue and/or special taxes. In times of economic recession the premium could be reduced and essential services maintained by cutting the budget in less pressing areas. Participation must be *compulsory* if we are to serve the whole population. Voluntary prepayment plans have never reached more than two-thirds to three-quarters of the population. They cannot afford to cover all risks for all subscribers; they have no elasticity with which to meet sudden changes in the business cycle and they cannot initiate a regional organization of comprehensive services. Voluntary schemes are unable to do anything for teaching and research which I am convinced must have access to some share of the medical care dollar.

This leads to two important implications of the foregoing which must be touched on—the cost of the program and who will control it. Since we possess no accurate figures on our total health bill, it cannot be said that a comprehensive plan, in the long run, will be a staggering burden or not. It depends on what we want. Britain's economy permitted it to start building new hospitals only a few years ago; yet, it is said, their revenue from taxes on alcohol and tobacco together would pay for two National Health Services! I suspect that North Americans are likely to wish full health services as they come to understand the benefits. What proportion of the gross national product should be devoted to health depends on our national scale of values. Political judgment will have to settle the competition between measures which promote the welfare of the entire population, our commitments internationally and frills.

The question of controls is too complicated for me to deal with here. In a democracy a major expenditure of public funds must come under the scrutiny of the legislature or a body subject to it. There are various ways of introducing degrees of insulation to ensure stability of support and to increase a measure of autonomy in technical matters, e.g. by special sponsorship by the Privy Council, by commission, etc. In the long run, in our society, we are committed to the view that governments act in the public interest and that we get the kind of government we deserve!

This matter is of the greatest concern to the medical profession which has expressed its opposition to government-controlled plans. Since there are so many possibilities for working out arrangements for representation of professionals to determine policy touching on the work of the interested professions, I see no value in a blanket opposition. In fact, I am confident that statesmen in Canadian medicine will not permit the considerable element of conservatism among their colleagues to block the way to a constructive policy for the benefit of the nation. I would emphasize how proud many of us are of the attitudes held officially by the Canadian Medical Association. Over several decades these have consistently been more liberal and at the same time more constructive than those of organized medicine in some other quarters of the globe.

A word on behalf of doctors in general may be called for. If one reads "Call the Doctor" by R. S. Turner, one will get a glimpse of the difficult time the profession has had in coming through the great social changes of the past two centuries, and now the assimilation of the new science has been a thrilling but preoccupying experience. The doctor has had to be an authoritarian; we insist that he carry tremendous responsibility and make arbitrary decisions. As he concentrates on the minutiae of function in the human individual, it is easy for him

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to miss seeing history flow around him. Again, correctives are developing in medical education and, with a high calibre of leadership in the national body, I think that we shall see Canadian medicine coming through this transition with our esteem maintained.

I would be charged with dodging hot issues if I overlooked the question of remuneration of the doctor. For many the fee-for-service relation between doctor and patient is the guardian of all kinds of considerations sacred to good medical care. This I regard as one of the cultural tenets dealt with earlier. There is no evidence that a salaried basis of service of itself disturbs the quality of medical care any more than does fee-for-service. Many of our leaders in medical education and in the Department of Veterans Affairs and Armed Services give exemplary medical care though virtually on a salaried basis. It may be that in Canada we can utilize the advantages of both systems. A substantial salary may be an inducement to doctors to serve in thinly populated areas or as specialists in secondary centres where the volume of work may be unpredictable. On the other hand, a component of income related to volume of service is a good way to reward the overworked doctor. The fee per item can be small enough to remove the temptation of overservicing, and large enough to reward the doctor who commands a larger following. In any case, only with a good salary component can one provide for income gradations to match increasing years of experience and additional postgraduate training. It also permits a merit award, determined by peers and community.

My final comment is on the role of the citizen in the health program. My experience with interested laymen on the boards of university, hospital and voluntary health agencies leads me to believe that apart from purely technical questions the doctor contributes best to the making and implementing of institutional policies when he serves with others on an equal basis. There is always need of the spokesman for the general public. The neutral, without vested interest, can see many issues in the best perspective. Some of our great medical centres received their main impetus from laymen devoted to education and medical care betterment. This is also an argument for the adult education movement which is possibly our best agent for experience in the democratic method. It is in the continuing education centres and groups for community studies that people are learning so well how to examine mutual problems objectively, how to use the knowledge and skills of experts and how to get around the obstacles of language. As stated in the Declaration and Principles of the World Health Organization, "informed opinion and active co-operation on the part of the public are of the utmost importance in the improvement of the health of the people".

CASE REPORTS

NITROGEN DIOXIDE— A RESPIRATORY IRRITANT

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THE DANGERS of inhalation of nitrogen dioxide and related fumes have been known for some time. In 1912, Wood[1] reported on fatal bronchiolitis obliterans due to nitric oxide, then a hazard in industrial and chemical laboratories.

In 1930, Nichols[2] described the pathological features resulting from the inhalation of gases generated by the decomposition of roentgen films of the nitrocellulose type. He felt that the nitrogen dioxide fraction was responsible, being a corrosive and deadly gas which in the presence of water or moisture liberated free nitric acid. Pulmonary edema of varying degree was a consistent feature and was often fatal within a few hours. Radiologically an exudative infiltrate was noted and interstitial fibrosis became apparent even within two weeks. Clinically, the picture was that of marked respiratory distress with cyanosis.

Von Oettingen[3] in 1941 referred to 175 fatalities due to nitrogen dioxide inhalation. Most deaths occurred within a few hours of exposure and were due to acute pulmonary edema. Deaths due to bronchiolitis obliterans occurred three to five weeks later. In more recent years a number of reports have come forward and the dangers of such fumes are no longer felt to be restricted to industrial occupations.

Lowry and Schuman[4] in 1956 gave the name "silo-filler's disease" to the syndrome encountered in farm-workers exposed to injurious nitrogen dioxide fumes while filling or re-entering a silo within a week of its being filled. Their first two cases were those of brothers exposed on the same day, with latent periods of 16 and 21 days, during

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which they were not entirely well, with death on the 30th and 27th days, respectively, following exposure. Histologically, there was an increase of blood and fluid but with micronodular lesions of bronchiolitis obliterans throughout. Cellular fibrin plugs were noted within the bronchiolar lumina—which became organized as progressive destruction of the wall occurred. They reported two other cases as well, and in addition to the features of time exposure, latent interval and the onset of a second phase, stressed the typical miliary appearance on the radiograph, with confluent lesions in advanced cases, the complete negativity of bacterial, mycotic and viral studies, and the poor response to antibiotics, oxygen and bronchodilators.

Roberts[5] described a pneumonitis due to a physical agent, nitrogen dioxide, causing early pulmonary edema and a subsequent bronchiolitis fibrosa obliterans with numerous discrete nodular densities. Gailitis, Burns and Nally[6] incriminated fresh silage and its fumes of nitrogen dioxide and its polymer nitrogen tetroxide. They described one case in which the radiographs were apparently normal. They considered that in addition to such cases of mild bronchitis and bronchiolitis, other types of bronchopulmonic injury included fatal pulmonary edema and bronchopneumonia and subsequent bronchiolitis fibrosa obliterans. They also described the sudden deterioration coming on after a latent interval of three weeks. The progressive elevation of the blood CO_2 level was felt to be a poor prognostic sign. Other cases were reported by Leib *et al.*[7]

In 1958, Dickie and Rankin[8] discussed the similarities and the distinctions between "silo-filler's disease" and the condition known as "farmer's lung". While there are similarities in the initial symptoms, radiographic appearances, recurrence on exposure, and residual pulmonary insufficiency, the differential features are significant. Farmer's lung is more frequently encountered, the exposure occurring on re-opening, after several months, of a silo containing mouldy hay, grain, fodder or silage. The presence of moulds is noted in almost all cases. There is less sputum and the patients experience recurrent difficulties during the winter months. *Candida albicans* is found in 50% of the cases. The condition of farmer's lung is essentially a granulomatous interstitial pneumonitis, despite an occasional relatively normal radiological appearance. The histological features include epithelioid cells, giant cells and occasional tubercles: in one case interstitial fibrosis was noted. The authors felt that it was due to a hypersensitivity response to the moulds or products of the moulds. The rapid onset of symptoms is totally unlike that which is generally encountered in fungus disease.

The oxides of nitrogen are derived almost entirely from inorganic nitrates in plants. Factors which increase plant nitrates are drought, highly nitrated soil and immaturity of the plant itself. There is a present-day trend towards increasing use of organic nitrates in fertilizing mixtures. Surprisingly large amounts of nitrogen dioxide gas are given off in the first week of silage fermentation.

The following is the case history of a 16-year-old boy who had been placed in a corrective institution in a rural area in April 1958.

Beginning in May, this boy carried out innumerable jobs around the farm. At first, his work often consisted in walking behind a fertilizer wagon, and the patient stated that he was always covered with fertilizer dust. In July, he worked for 4-5 days over a period of two weeks, for a couple of hours each day, in filling a silo. His work consisted in channelling the grass up a chute into the top of a silo and then going inside the silo and stamping it down. He noted "a funny odour" at the time but experienced no acute symptoms.

Approximately four weeks before admission, he burned a can of shoe polish in an enclosed basement of the institution. A tremendous amount of black fumes was produced and he experienced a burning of the eyes, difficult breathing and intense coughing. These symptoms disappeared after he had been out in the fresh air for approximately 15-20 minutes. He promptly returned inside, as apparently the object of the prank was to determine who could tolerate the fumes for the longest period of time. Symptoms began 10 days before his admission when he experienced fever and chills which lasted for two days. He was then relatively well for four days, after which he developed another chill, fever, dyspnea and severe cough. He was treated at the institution's infirmary with penicillin and streptomycin for three days and was then transferred to the Hôtel-Dieu Hospital of St. Jerome, Quebec, on November 30, 1958.

His past history revealed that he had been hospitalized in 1950 for a period of eight months, in another institution, with a diagnosis of erythema nodosum and pulmonary tuberculosis. His family history was negative for tuberculosis. An Old Tuberculin test (1/10,000) was positive. Chest radiographs on that admission revealed a left hilar enlargement with perihilar infiltration. After one month in hospital, he developed clinical and radiological evidence of a left-sided pleural effusion. At this point, despite the lack of bacteriological confirmation of tuberculosis, he was started on streptomycin and para-aminosalicylic acid, the pleural effusion clearing within seven weeks. Bronchoscopic examination was negative. Sputa and gastric washings were never positive for acid-fast organisms. His discharge diagnosis was: "probable pulmonary tuberculosis, minimal, apparently arrested".

On admission to the Hôtel-Dieu Hospital, St. Jerome, on November 30, 1958, the boy was cyanotic and in obvious respiratory distress with dyspnea, orthopnea, persistent coughing which was mostly non-productive but occasionally was productive of sputum tinged with blood, and complaints of right-sided chest pain. His temperature was 99.4° F., his blood pressure 110/70 mm. Hg, pulse 92/min. and quite regular, and his respirations were 36/min. Examination of the head, ears, eyes and throat was essentially negative. There was no thyroid enlargement and no palpable adenopathy. His heart sounds were normal and no murmurs were heard. Examination of the lungs revealed moist rales at both

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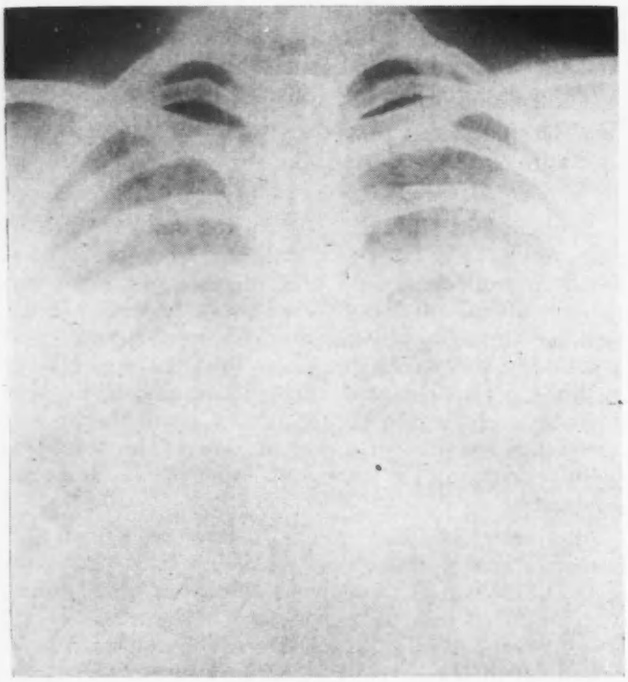

Fig. 1.—Admission radiograph, November 30, 1958. Dense non-homogeneous opacity, covering the lower two-thirds of both lung fields, is seen. No evidence of atelectasis or pleural fluid is present.

bases and a friction rub at the right base. Abdominal examination was not contributory.

His hemoglobin was 12.9 g. % (87.7%): hematocrit, 49%: leukocyte count 18,700 per c.mm. with polymorphonuclears 86%, basophils 1%, monocytes 1%, and lymphocytes 12%. The sedimentation rate was 31 mm. per hr. Urinalysis was normal. His non-protein nitrogen value was 45 mg. %. Repeated examination of sputum by direct smear failed to reveal acid-fast organisms, fungi or other bacteria. Cultures were subsequently reported negative for *Mycobacterium tuberculosis* and fungi. The CO_2 level was 36 vol. %. His chest radiograph on admission (Fig. 1) revealed bilateral confluent opacities radiating outwards in butterfly fashion from the hilar regions. The diagnostic impression at this time was bilateral bronchopneumonia.

His temperature climbed rapidly to 103° F. and despite oxygen therapy his respiratory distress increased. Because of the history of possible tuberculosis, he was started on streptomycin, Rimifon and para-aminosalicylic acid. Tetracycline and chloramphenicol were added to cover the possibility of a bacterial infection. He was also digitalized. He continued to cough frequently and remained febrile for 10 days with a coincident tachycardia. He received oxygen continuously for two weeks but remained moderately agitated; the cyanosis did not diminish and the radiological appearance was essentially unchanged (Fig. 2).

Surgical consultation was requested on December 15. At this time, the patient was afebrile, but still cyanotic when not receiving oxygen. He demonstrated clubbing of the fingers, and moist rales could still be heard at both lung bases. Clinical improvement was slow to start but by the 27th hospital day was unmistakable; radiographs (Fig. 3) for the first time showed improvement, the lesions being less confluent but with innumerable small nodular densities scattered throughout both lung fields.

Further laboratory tests carried out about this time revealed a thrombocyte count of 311,000 per c.mm., a bleeding time of 45 sec. and a coagulation time of 5 min. 52 sec.; his prothrombin was 89% and a Rumpel-Leede test was negative. Bronchoscopic examination revealed only slight mucosal hyperemia. By January 9

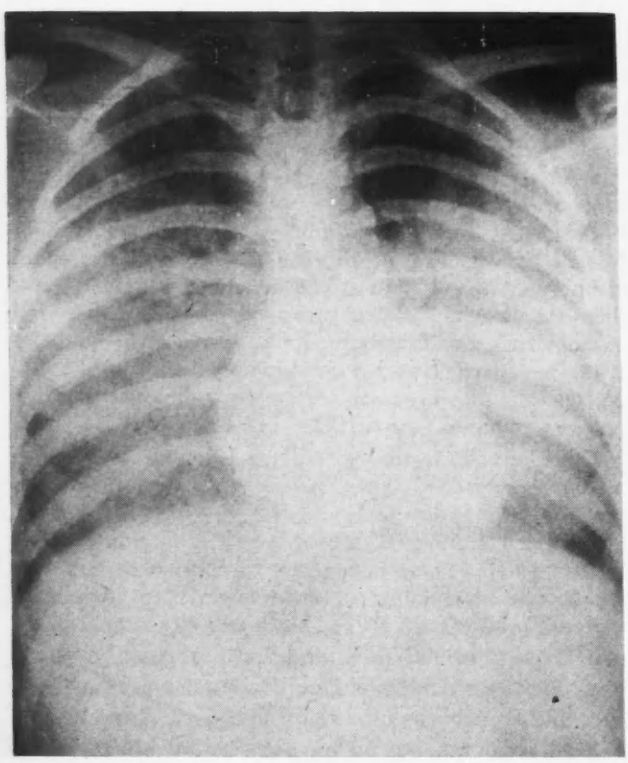

Fig. 2.—December 4, 1958. No apparent change since the first radiograph, but the technique used is different. This overpenetrated radiograph shows some calcified lymph nodes in the left hilum.

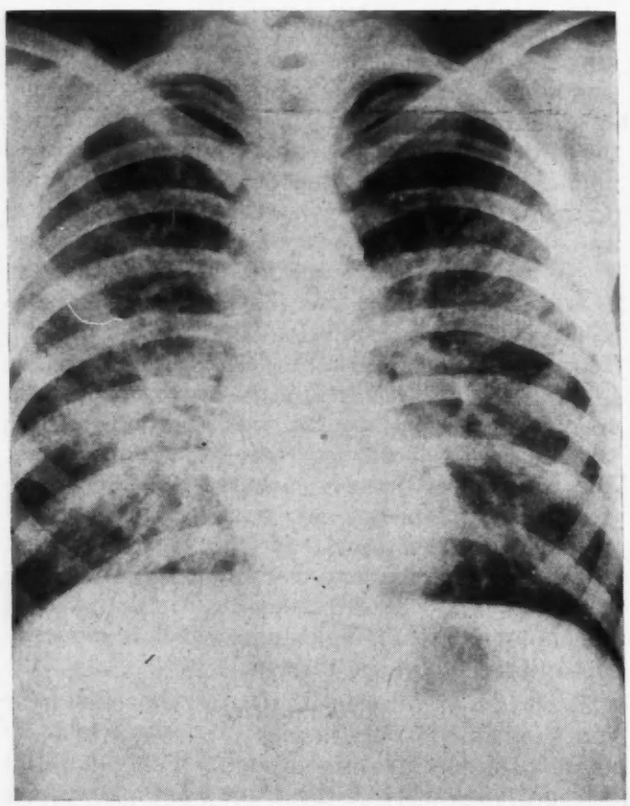

Fig. 3.—December 26, 1958. Partial clearing of the diffuse bilateral condensation is shown.

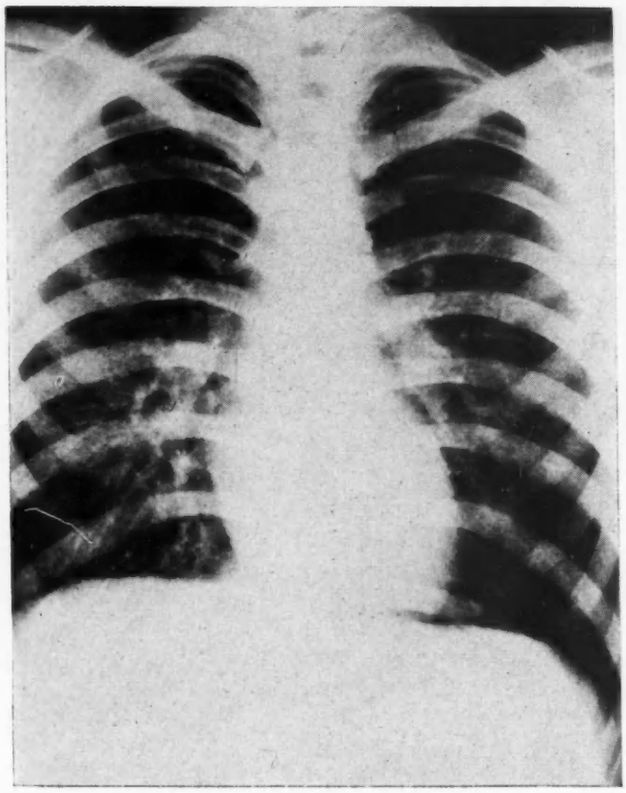

Fig. 4.—January 9, 1959. Some increased linear markings, congestive in appearance, are still visible on both sides.

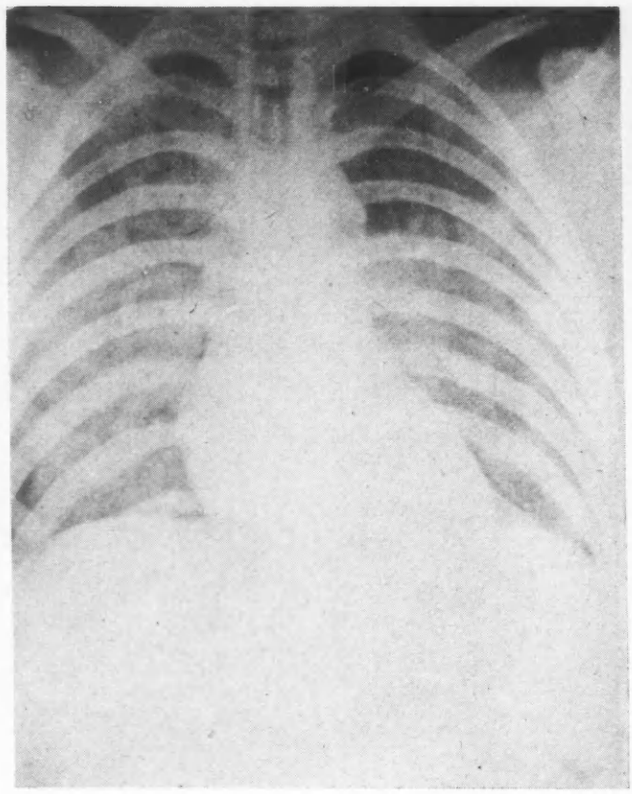

Fig. 5.—January 12, 1959. Radiograph was taken four hours postoperatively. The radiological appearance is quite similar to that in Fig. 2.

(41st hospital day) there was radiological evidence (Fig. 4) of significant resolution of the lesions but with persistence of the micronodular densities. The patient was afebrile, acyanotic, ambulatory and free of respiratory distress.

On January 12, a biopsy of the lingula was performed through a limited thoracotomy incision. Following pre-medication of 1/8 grain morphine and 1/200 mg. atropine, the patient was given 500 mg. of sodium thiopental and 100 mg. of Flaccadil intravenously, then intubated and maintained on nitrous oxide, oxygen and cyclopropane.

The operation was quite well tolerated by the patient. However, four hours after the operation, he exhibited a clinical picture quite comparable to that on admission and (Fig. 5) showed a recrudescence of the pulmonary lesions in butterfly formation, with marked congestion of both lung fields, not quite as marked, however, as on his admission. The patient remained febrile for the first three postoperative days, his temperature being approximately 101° F. He was cyanotic and dyspneic and demonstrated a tachycardia which lasted for the same period. Some blood-streaked sputum was expectorated during the first few days. Rales were noticed in both lung fields, especially at the left base. The chest drain was removed on the second postoperative day. Again a spontaneous resolution without any specific treatment was noted on the fourth postoperative day. Progressive improvement was then seen. Radiographs on January 16 showed a slight shift of the mediastinum towards the right owing to a partial atelectasis at the right base. Films on January 26 showed 95% clearance of the lesions in both lung fields (Fig. 6). The patient was discharged from the hospital on January 29, 1959, and was feeling quite well at that time.

The pathological specimen was triangular in shape and measured 2.5 x 1 x 2.5 cm.; the pulmonary parenchyma was firmer than normal on palpation. On cut

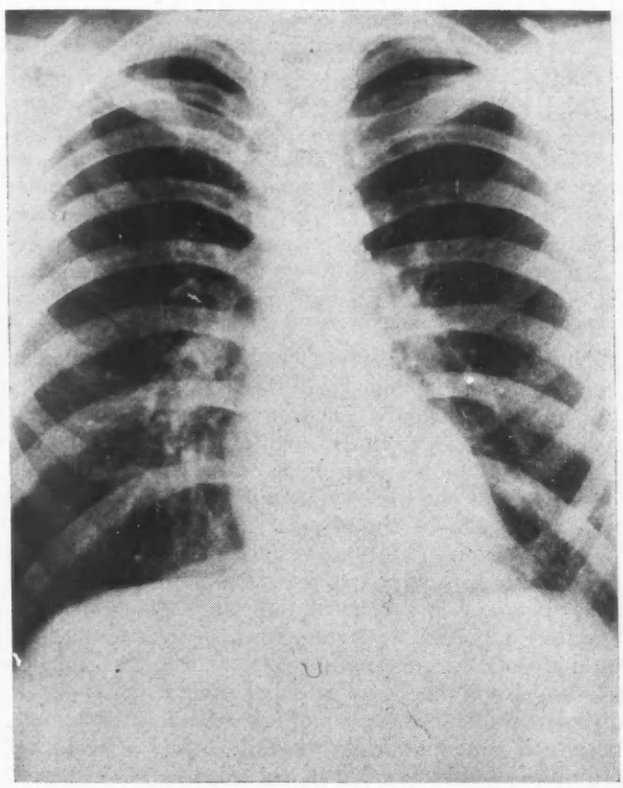

Fig. 6.—January 26, 1959. This radiograph was taken prior to discharge. There is a persistence of some linear and nodular opacities, congestive in appearance, in the right perihilar region and the middle third of the left lung. A small hazy density is noted in the region of the lung biopsy.

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Fig. 7.—Edema and blood are present within the alveoli. The exudate under low-power magnification resembles superficially the exudate in alveolar proteinosis.

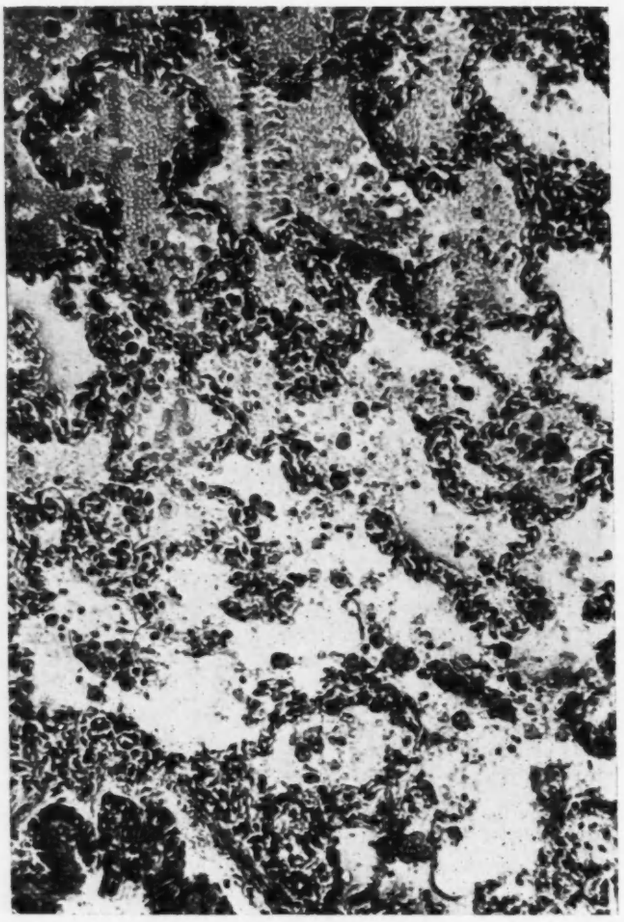

Fig. 8.—High-power magnification. Edema, blood and macrophages are shown within the alveoli.

section, the parenchyma was light brown in colour but innumerable small zones of non-aerated tissue of dark brown colour were noted, measuring 0.5 x 0.8 cm.

Histological examination revealed alveoli filled with edematous fluid and blood. The septa were thickened, fibrous and discretely infiltrated by lymphocytes and plasmacytes. In other areas the septa were distended with edematous fluid. The lumina of some alveoli and terminal bronchioles were almost completely blocked with young fibrous tissue, encircling in certain areas macrophages and the lining cells of the alveolar walls (Figs. 7 to 10).

The differential diagnosis based on the histological appearance at the time of initial examination included pulmonary edema, alveolar proteinosis, interstitial pneumonitis evolving towards a diffuse interstitial fibrosis (Hamman-Rich syndrome) or again a pneumocystic pneumonia of chronic or abortive type. Since there was no PAS uptake by the alveolar exudate, pneumocystic pneumonia and alveolar proteinosis were thereby eliminated. In addition, the clinical history of sudden onset was not in favour of this latter diagnosis. This view is supported by Rosen,[10] who contends that the intra-alveolar edema with desquamated macrophages in the alveoli has only a superficial resemblance to alveolar proteinosis, a condition which he originally described, and that while the radiological appearances are quite similar, the clinical evolution is quite distinct.

These lesions were thus compatible with an interstitial pneumonia with alveolitis and bronchiolitis obliterans, caused by the inhalation of an irritating and toxic gaseous substance, which provoked an intensive exudative response within the alveoli and terminal bronchioles, with a fibrinous material, which, in certain areas, undergoes organization.

DISCUSSION

The pulmonary changes subsequent to nitrogen dioxide inhalation, while known for several decades, have been recognized only in recent years as occurring outside industrial occupations. The syndrome known as silo-filler's disease was originally described in 1956.

In the case under discussion, the diagnosis was not established until the lung biopsy was made. The past history of possible pulmonary tuberculosis served to becloud the issue. Only when the unusual histological picture was encountered did further exhaustive interrogation of the patient reveal that he had, in fact, been exposed to nitrogen dioxide and related fumes on four different occasions, the first known exposure being while working with fertilizer, which, as already stated, contains organic nitrates. Since he was covered with this fertilizer dust, we can safely assume that he inhaled some of this dust which on contact with the moisture in his respiratory passages became an injurious physical agent. The second exposure undoubtedly occurred when he was employed in filling a silo. The third exposure was when, as a prank, he burned a

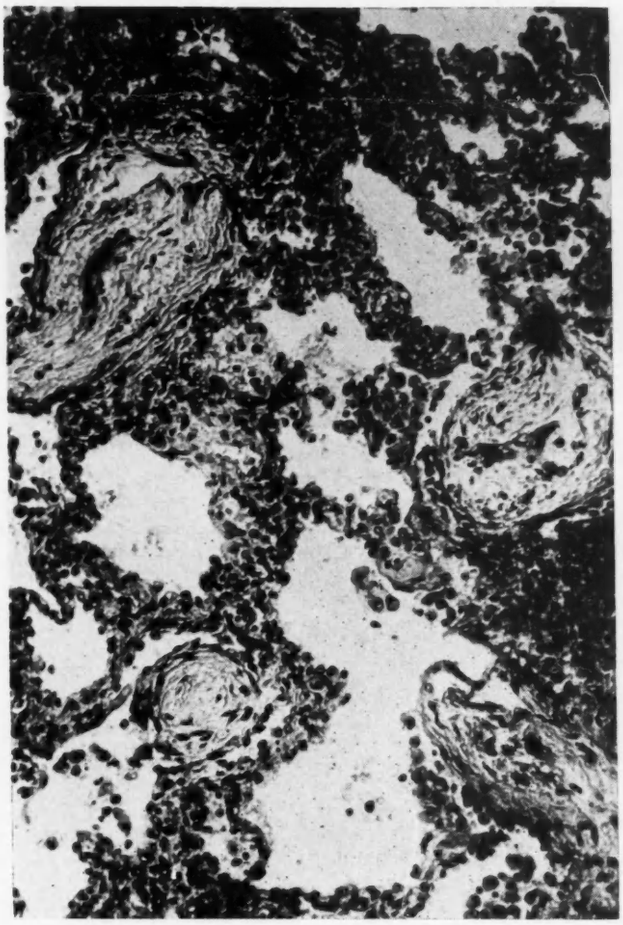

Fig. 9.—Alveoli and terminal bronchioles are almost completely obliterated by nodules of young connective tissue lined by an epithelium. Note the thickening of the septa which are infiltrated by lymphocytes and plasmacytes.

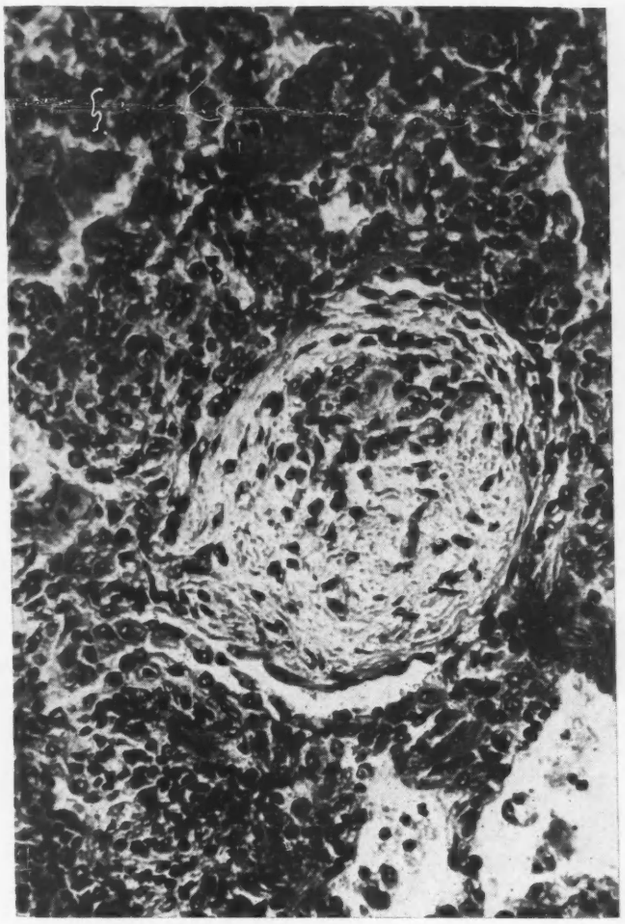

Fig. 10.—High-power magnification. Note nodule of young connective tissue engulfing a few macrophages at its centre, and the inflammatory interstitial infiltrate.

can of shoe polish. Shoe polish contains nitrites and nitrobenzine and the irritating fumes certainly contained a high proportion of nitrogen dioxide. The fourth exposure was iatrogenic in nature, when unwittingly before the diagnosis was suspected nitrous oxide anesthesia was used for the lung biopsy and resulted in a severe recrudescence of the clinical and radiological findings within 3-4 hours of the operation.

In the case presented, recovery was slow but essentially spontaneous, since we have no reason to believe that the antibacterial drugs used exerted any influence except perhaps to prevent secondary infection.

When the diagnosis is suspected and tuberculosis can be eliminated, a course of corticosteroid therapy may be helpful in bringing about an early remission. Recommended doses of prednisolone are 16 to 24 mg. per day.

SUMMARY

The literature, to date, of the dangers of nitrogen dioxide inhalation as encountered in the syndrome known as silo-filler's disease is reviewed.

An unusual case is presented in which the diagnosis was beclouded by a past history of possible tuberculosis, and where four different probable exposures occurred. Radiological evolution and histological sections are included.

The danger of using nitrous oxide as an anesthetic agent in such cases is made clear. Suggested treatment in suspected cases is outlined.

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NONSPECIFIC GRANULOMATOUS DISEASE OF THE STOMACH WITH HEMATEMESIS FOLLOWING RESERPINE THERAPY

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G. BERRY, M.D.,† *St. Jerome, Que.*

CHRONIC GRANULOMATOUS inflammation is a defence mechanism of the organism mediated through the reticuloendothelial system. Agents which are capable of provoking such reactions are numerous and include bacteria, viruses, foreign bodies and many others.[1] In recent years, various authors have described the occurrence of granulomatous lesions in association with hypersensitivity phenomenon.[2, 3] The typical granuloma is described as having a central area of epithelioid cells, with or without giant cells, surrounded by lymphocytes, plasmacytes and fibroblasts. Such reactions in the stomach are rare and we feel that such a case merits reporting.

The patient was a 59-year-old white French Canadian woman who was known to have suffered from essential hypertension for many years, with blood pressure readings ranging from 220/110 mm. Hg to 240/140 mm. Hg. Her physician prescribed reserpine in doses of 25 mg. four times daily. After four days of this treatment the patient had an attack of severe epigastric pain, acute in onset and associated with nausea, massive hematemesis and loss of consciousness. On arrival at the hospital her hemoglobin level was 6 g. per 100 ml. and her hematocrit was 18%. After having received 1000 c.c. of whole blood, the patient continued to vomit fresh blood and was prepared for emergency laparotomy and gastrectomy. This patient had never suffered symptoms referable to any disorder of the gastrointestinal tract prior to this event.

The surgical specimen received at the laboratory consisted of a stomach measuring 12 cm. along the greater curvature and 8 cm. along the lesser curvature. There was no sign of ulceration macroscopically. The mucosa of the antral area was edematous and spotted by fine petechiae. On macroscopic section the submucosa was thicker than normal owing to infiltration by blood and edema. Histologically, no mucosal ulceration was evident; however, a marked granulomatous inflammatory infiltration was seen between the mucosa and submucosa. This infiltration consisted of epithelioid cell masses with a central foci of giant cells, surrounded by lymphocytes, plasma cells and eosinophils (Figs. 1 and 2).

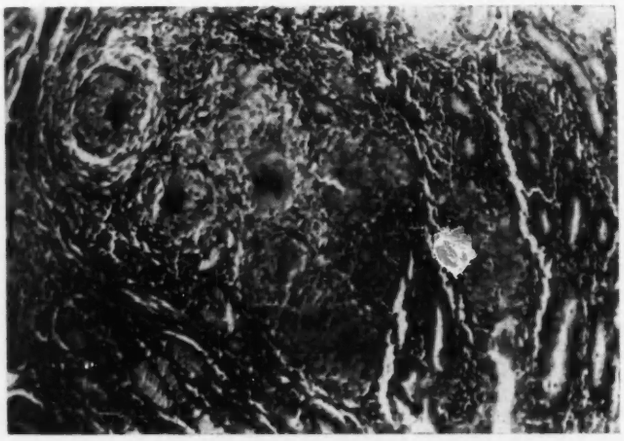

Fig. 1.—Granulomatous lesions in the gastric mucosa.

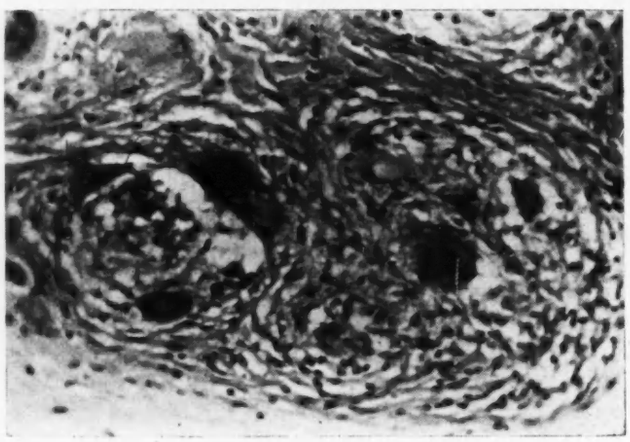

Fig. 2.—Granulomatous lesions in the gastric submucosa.

COMMENT

Other cases of hematemesis and melena following therapy with reserpine[4] have been reported in the literature. These have been ascribed to the inherent action of this drug on the gastrointestinal tract, i.e. to hypermotility and increased acidity due to hypersecretory action of the drug, with resulting reactivation of dormant peptic ulcers, acute peptic ulcer formation in a heretofore intact mucosa, or continuous mucosal weeping of blood, as this case would suggest.

Defects in blood coagulation have also been implicated as the cause of bleeding in such cases. However, Hollister[4] was unable to substantiate this hypothesis. In some receiving large doses of reserpine, a lowering of the platelet level has been found,[5] but in such cases one would anticipate manifestations of a systemic hemorrhagic diathesis rather than one localized to a particular organ.

We have not encountered in the literature any previous reports of granulomatous gastritis with hematemesis associated with the administration of Rauwolfia alkaloids. Clinically, symptoms referable to an entity termed "allergic gastritis" have been described.[2, 6] It would seem that in the case described in this report, this type of gastritis was a manifestation of hypersensitivity to this drug.

We would like to thank Dr. P. M. St. Pierre, who has kindly allowed us to publish his report of his patient.

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†Visiting physician, Hôtel-Dieu of St. Jerome, Que.

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SHORT COMMUNICATION

A USEFUL BANDAGE-SUPPORT MADE OF VELCRO AND ELASTIC (VELASTIC)*

G. DOUGLAS TAYLOR, M.D.,† *Toronto*

A COMBINATION of ordinary "ladies' wear" elastic and the double self-locking nylon material, Velcro,®‡ makes a very convenient bandage or support with numerous uses. These include the provision of supports for weak or painful joints, or for holding protective splints, or collars, in place. Such Velastic® bandages are inexpensive, long-lasting, adjustable and are easy to apply and remove. They are made simply by attaching a small matching piece of the interlocking Velcro to each end of a strip of elastic. During each application the two Velcro materials, on contact, interlock and hold firm; and for removal they may be peeled apart with little or no effort. Velastic bandages are useful as simple supports for weak joints, for sprains or strains, or for joints with synovitis or arthritis. They provide a satisfactory alternative for sticky adhesive tapes or the usual elastic-type tensor bandages. In the application of splints or collars for arthritic or injured joints they are much more convenient than the time-consuming method of winding and unwinding ordinary flannel or cotton bandages; and they are more readily adjustable than tapes and buckles.

MATERIALS

Velcro‡ is made of nylon, and consists of two parts, each one on a similar tape-like base but each with a different surface structure: one portion that feels slightly rough, has rows of tiny *hooks*; the other, that feels soft and fluffy, contains numerous tiny loops, and is known as the *pile*. When in contact, with even the slightest pressure, the Velcro parts interlock so tightly that they can hardly be separated by a straight pull and yet they can be detached readily merely by grasping an edge and peeling apart. Velcro may be washed and used repeatedly without apparent deterioration. Two-inch lengths of Velcro have been found to be sufficient for most of the bandages required.

Elastic is available in various widths, colours, and degrees of strength or elasticity (obtainable in most dry-goods or department stores). The 2-inch width and pink colour have been found suitable for most bandages. Their length will depend upon the use for which they are required. When elasticity *per se* is not required, as in a binder or restrainer, the Velcro may be attached to the ends of almost any type of material, such as plain tape, flannel, cotton, or leather.

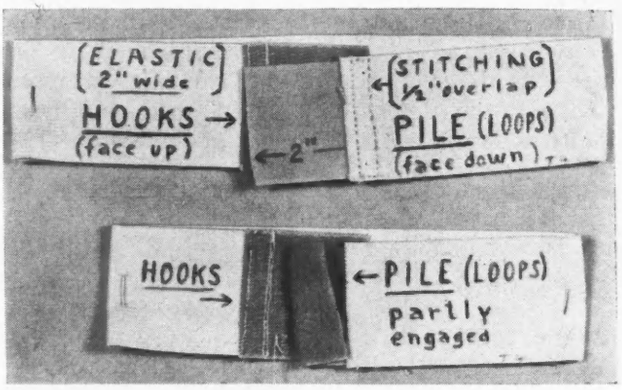

Fig. 1.—The "Velastic" bandages show 2 inches of each of the Velcro parts (hooks and pile) stitched to the ends of pieces of 2-inch wide elastic, with a ½-inch overlap. In the upper bandage the Velcro parts are in contact, interlocked; in the lower bandage the Velcro parts are only partly engaged, with the pile partly peeled off.

TECHNIQUE IN MAKING A VELASTIC BANDAGE

1. A strip of elastic is selected, about 2 inches *shorter* than the desired *total* over-all length of the finished Velastic bandage. This allows for incorporation of the Velcro ends, and the overlap for sewing.

A 2-inch piece of Velcro "hooks" is sewn, by hand or machine, *facing up* on one end of the elastic with an overlap of ½ inch. The other part of the Velcro, 2 inches of the "pile", is sewn *facing down*, on the other end and *opposite side* of the elastic, also with a ½-inch overlap. Thus when applied around a joint, the hooks and the pile meet face-on and part or all of the full 2-inch surface of each may be utilized in the interlocking process. (For example, in an 8-inch bandage there are 2 inches of hooks, 2 inches of pile, and 5 inches of elastic. This totals 9 inches, but with the two ½-inch overlaps for sewing the total over-all length is 8 inches.)

There are numerous variations to this procedure, e.g. for greater interlocking strength or adjustability the length of the Velcro (either the hooks or the pile, or both) may be increased; for wider bandages or for binders two or more pieces of Velcro may be used, side by side, either separate or sewn together; and the Velcro may be sewn crosswise or at an angle on the elastic or other material. To attach the Velcro to the elastic, as an alternative to sewing, other

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‡The Velcro used in the development of these Velastic bandages was kindly donated by the B. C. Hollingshead Co., Toronto, the Canadian distributors of Velcro for medical, hospital, and other health or first-aid uses.

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methods may be used, e.g. staples, pins, lacing, hooks, or a special glue-like adhesive. If for any reason it is considered undesirable to permit the Velcro nylon material to touch the patient's skin it may be attached to the elastic with complete overlapping, so that only the elastic comes in contact with the skin. To prevent "catching" on nylon stockings the Velcro may be trimmed slightly so that it will not reach the edges of the elastic. This technique may well become the method of choice for most of these Velastic bandage-supports.

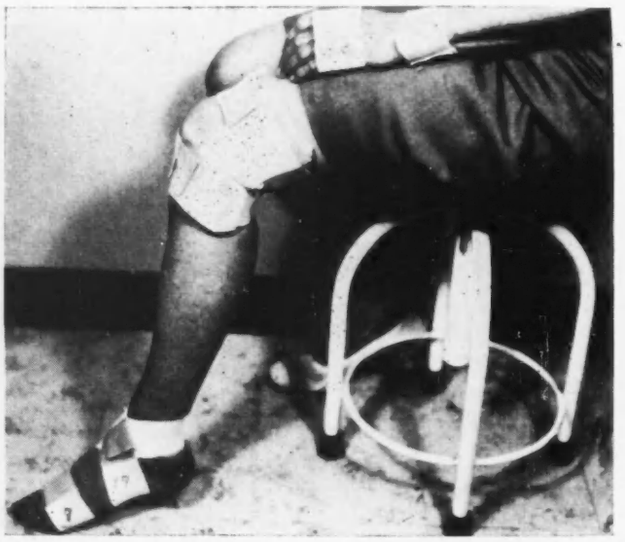

Fig. 2.—Six Velastic bandages are shown in use. At the knee they hold in place two covered felt pads. The figures indicate the total over-all length of each bandage, in inches, as follows: metatarsal cuff, 9; figure-of-eight ankle bandages, 19; for knee supports, 13 and 17; for the hand, 8, and the wrist, 7.

APPLICATION

Application of a Velastic bandage-support is simple, easy, quick, and should be foolproof. The bandage is placed over the joint or splint with the Velcro hooks facing up, away from the skin or stocking; the elastic is wound around the joint or splint to any degree of tightness desired; then the Velcro pile is pressed gently down on the hooks, with immediate interlocking. For removal, one edge of the pile is simply grasped and peeled off.

The following are some specific examples of the purposes for which Velastic bandages may be employed as simple supports or as a means of holding splints or collars in place. The number depicted on each bandage in the illustrations indicates its total overall length.

A. As a *support*, with or without felt pads, for weak or painful joints (Fig. 2).

1. In the foot, to provide support for weak arches: (a) As a *metatarsal cuff* to prevent splaying. If desired, a metatarsal pad may be incorporated and attached inside the elastic by taping or other means. The length of this bandage may vary from 8 to 10 inches (that in the accompanying illustration is nine inches in length). (b) Around the mid-foot as a binder, or alternatively to hold in place some other type of support for the long arch. The length of this bandage varies from 9 to 12 inches.

2. On the ankle: (a) used as a simple "figure of eight" bandage it provides a very effective support. The usual lengths are 18 to 21 inches (19 inches in the illustration). (b) A more complicated support may be made as follows: one Velastic bandage is placed around the ankle just above the level of the malleoli, meeting at the mid-line anteriorly, with or without a small felt pad beneath it. On the outer surface of this elastic, over each malleolus,

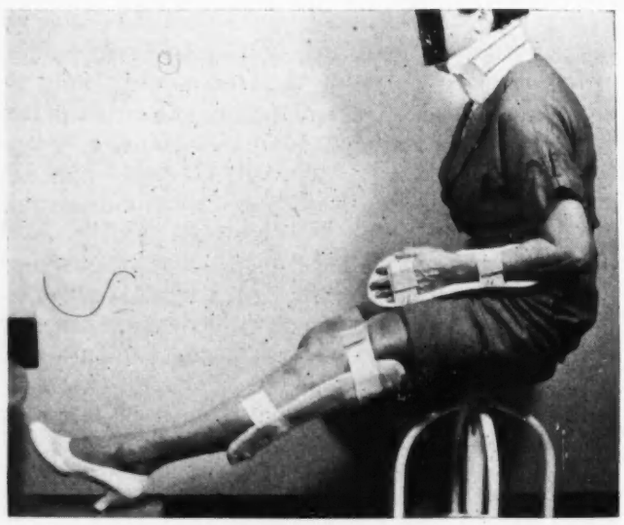

Fig. 3.—A moulded plaster knee-splint is held in place by Velastic bandages of 13 and 17 inches; and an aluminum hand-splint, by bandages of 12 and 11 inches. A plaster collar is held by a Velastic bandage of 19 inches, interlocking in front.

are attached additional small (2-inch) pieces of Velcro *pile*. A second Velastic bandage, with *hooks* on both ends, is attached to these Velcro side-pieces, with the elastic passing over the malleoli and under the heel. Being adjustable, this has some advantages over the usual one-piece ankle-support.

3. For the knees, a simple and practical support is made as follows: two slabs of firm felt, ½ inch thick and approximately 9 to 10 inches long and 4 to 5 inches wide, are cut so that they are 1 inch narrower in their middle one-third. These are then covered with stockinette (Fig. 2). The slabs are placed lengthwise along the inner and outer aspects of the knee and the ends are held in place by Velastic bandages, one below and one above the patella. This allows for flexion and extension of the knee without any creasing of the bandages and without any pressure over the popliteal region.* The lengths of the bandages usually vary from 13 to 18 inches.

4. On the elbow: a convenient support can be provided by two small felt pads, somewhat similar to those used for the knee, with Velastic bandages applied above and below the joint.

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*Supports of this type have been used for many years, but usually are made of sponge-rubber held in place with numerous layers of elastic or tensor bandages, which often are difficult to hold in place and which tend to crease behind the knee.

5. On the wrist or hand: the Velastic bandage alone provides a very satisfactory support for the wrist. Also, when placed across the metacarpophalangeal joints the bandage, alone or with a felt pad, aids in preventing strain and ulnar deviation, as may occur in rheumatoid arthritis. The lengths of these bandages vary from 7 to 9 inches.

B. Velastic bandages provide a most convenient method to hold in place the splints or supports that almost always are necessary for the intermittent immobilization of painful or swollen joints in various types of arthritis or tenosynovitis (Fig. 3). Ordinarily, such splints are held in place by bandages which require considerable time and effort for winding and unwinding. In contrast, Velastic bandages require only one turn around the joint or limb with easily applied contact of the two Velcro interlocking surfaces, and a simple peeling apart for removal. In most cases this procedure may be carried out by the patient, without assistance. (1) For a single splint on a peripheral joint, such as the hand, wrist, elbow or knee, usually only two Velastic bandages are required, one above and one below the joint. Occasionally, in the case of a heavy person or a heavy splint, the Velastic bandage should be doubled or the Velcro should be attached to some non-elastic material such as tape, belting, or flannel. The length of the bandage varies; in most cases it will be from 1 to 4 inches longer than the circumference of the limb at the site of application, and, of course, it will depend upon the width or thickness of the splint. (2) To hold in place cervical collars prepared from various materials it is convenient to have the Velastic bandage fasten in front. The length of bandage used for this purpose usually varies from 18 to 23 inches.

C. For "emergency" use, two or more Velcro bandages may be attached to each other for any increased length required, e.g. to make a sling for support of the forearm, or to splint the upper arm to the chest for relief of a painful shoulder.

These Velcro and elastic (Velastic) bandages were conceived and developed in the Arthritis Clinic of a Geriatric Centre, primarily to provide a bandage-support that would be easy for the patients' feeble hands to apply and remove. Another objective was to eliminate the inconvenience and waste of time entailed in the winding and unwinding of the usual types of bandages by nurses and attending staff. It quickly became apparent that Velastic bandages have multiple practical uses and many advantages over plain flannel, tensor or adhesive bandages, especially since they are so readily adjustable and durable. Furthermore, they are easy for anyone to apply and to remove. In most cases this can be done by the patient himself. A supply of these bandages, in assorted lengths, can serve many useful purposes. For emergency use, a Velastic bandage can be made simply and quickly with two small pieces of Velcro, a strip of elastic and two pins. Their value in the home, arthritis clinic, hospital and convalescent institutions has been established. They should also prove to be useful in first-aid units, in sports and industry.

SUMMARY

The double interlocking nylon material known as Velcro, when combined with ordinary ladies'-wear elastic makes a most convenient, versatile and long-lasting bandage-support. These are useful either when applied alone as supports for weak or painful joints, or to hold in place splints or collars for arthritic joints. A simple method of making these Velastic bandages is described and illustrations are provided to demonstrate some of their uses.

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

TREATMENT OF TYPHOID FEVER BY VACCINES

In dealing with typhoid fever our most important duty lies in its prevention. Besides the hygienic measures, which should be enforced by the state, the method of prevention by vaccination has assumed, during the past decade, an important place in the prophylaxis of this disease. It was first used by Wright in 1896 on a few cases, and was then employed in India on four thousand cases with encouraging results. On the outbreak of the Boer war in 1898 it was extensively used on the troops leaving for the front. The results and records of these cases were unfortunately much confused, so much so, in fact, that the method was abandoned. Leischmann, however, continued its use among the European soldiers in India with brilliant results. The incidence per thousand was reduced from 28.3 per cent to 3.8 per cent, and the mortality per thousand from 4 per cent to 0.37 per cent. In fact the incidence and mortality were ten times greater in the unvaccinated than in the vaccinated troops. It is astonishing to note that the incidence in the vaccinated cases is less than the mortality in the unvaccinated. In the German South African army similar encouraging results have been obtained. Thus from an experience of some thirteen thousand vaccinated cases and sixteen thousand controls the prophylactic value of typhoid vaccination has been established.

Richardson has taken advantage of this protective inoculation to prevent the so-called hospital typhoid fever amongst the nurses and doctors and other hospital attendants in the Massachusetts General Hospital. In former years it was found that from two to six nurses had annually contracted typhoid fever within the hospital. In order to prevent this all the hospital personnel were submitted to anti-typhoid inoculation. Since then no cases of typhoid fever have developed amongst the attendants.—John C. Meakins and Lowell S. Foster: *Canadian Medical Association Journal*, 1: 496, June 1911.

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(Information regarding contributions and advertising will be found on the second page following the reading material.)

FITNESS FOR FLYING ON PASSENGER AIRLINES

OVER the past 20 years passenger flying on commercial airline carriers has increased 2600%. The steadily growing number of persons who fly as passengers on scheduled flights is bound to include a proportion who suffer from various clinical disabilities. Although on occasion air travel may be deleterious and inadvisable for such persons, in an increasing number of instances it is found that flying is the most satisfactory form of transportation for properly selected and prepared patients. In the interests of potential passengers with medical disabilities and of the public in general, it is necessary and desirable that medical criteria be defined to assist and provide guidance in the proper selection of patients for transportation by passenger airlines. Such criteria have recently been elaborated in a comprehensive and far-ranging report issued jointly by the Committee on Aerospace Medicine of the American Medical Association and the Committee on Medical Criteria of the Aerospace Medical Association.[1, 2] The contents of this report are recommended for the attention of all physicians, since any doctor today, regardless of his sphere of practice, is likely to be called upon to advise patients whether they should or should not travel by air. Owing to unfamiliarity with physiological conditions of commercial flight, many physicians unnecessarily advise certain patients not to fly, thereby depriving them of the advantages of economical, speedy, comfortable and safe transport. Intelligent guidance, advice and reassurance can go far in preventing medical and surgical difficulties in flight. Reprints of the joint statement entitled "Medical Criteria for Passenger Flying" may be obtained from the Department of Occupational Health, the American Medical Association, until such time as the stock of these documents is exhausted.

The following basic criteria should be considered when any patient is under consideration as a potential passenger on a commercial airline: (1) Is the patient able to travel by *any* means of transportation? (2) Would his presence in a passenger aircraft be offensive to other passengers? (3) Is the patient's condition sufficiently stable that it is unlikely to require an inconvenient and costly, unscheduled emergency landing and interruption of the flight schedule? (4) Is the patient's desire to travel by air based on valid reasons and not solely on such emotional factors as a wish to return home to die or to visit some shrine in the hope of a miraculous cure?

The joint report of the A.M.A. and Aerospace Medical Association points out that the long-held principle that any person who looks normal, feels normal, smells normal and can walk up the steps of a ramp can fly without likelihood of difficulty, is equally true today and may be made even more liberal since the advent of pressurized aircraft.

In deciding on any individual's fitness for passenger flying it is essential that the assessing physician possess some knowledge of basic operational data of the aircraft involved, such as its speed and duration of flight, the simulated altitude within the cabin, the availability of oxygen and the ability of the cabin attendants to take care of medical emergencies. Such data are tabulated in detail in the A.M.A.–Aerospace Medical Association report, as they apply to some of the commonly used passenger aircraft.

Certain conditions associated with flight must be considered in the light of their physiological effects on passengers, particularly those with clinical disorders that may impair normal physiological responses. Disturbances that result from changes in barometric pressure are now referred to by the term *dysbarism*. Such disorders include barotitis media, barosinusitis, aeroembolism, aerodontalgia and expansion of gases in the viscera. Persons predisposed to these flight complications include those with inflammatory edema of the nasopharyngeal orifice of the Eustachian tube, upper respiratory tract infections in general, congenital nasopharyngeal deformities, defective dental fillings, caries and periapical abscesses, various pathological lesions of the gastrointestinal tract, pneumothorax or pneumomediastinum, and individuals who have recently been subjected to pneumoencephalography or ventriculography.

Patients with impairment of cardiopulmonary function or of oxygen transport, from any cause, must be carefully selected and prepared for air travel, owing to the potentially dangerous effects of even minor degrees of hypoxia resulting from the reduction in alveolar oxygen pressure which is associated with the decreased barometric pressure at high altitudes. Before advising any patient that he is fit to fly, it should be ascertained that there is no interference with the supply of an adequate volume of oxygen to his lungs, and that there is no obstruction to the mechanical expansion of gases in his body passages, cavities or viscera.

The passenger should not impose any untoward effects upon the sensibilities, security and health of his fellow travellers. Persons with malodorous conditions, gross disfigurement or other unpleasant characteristics should not be transported by commercial passenger flights unless their isolation can be assured; nor should individuals with contagious diseases, those who are acutely or critically ill, or those who cannot take care of their own physical needs unless accompanied by suitable attendants. Persons whose behaviour might be disturbing or hazardous to other passengers should not be considered fit for travel on scheduled flights.

Patients with congestive heart failure, recent myocardial infarction or diminished cardiac reserve due to any cause should travel by air only if oxygen is immediately available. Generally speaking, if such patients can walk 100 yards and climb 12 steps without severe dyspnea or other distressing symptoms, flight in pressurized aircraft is permissible. Persons with a history of thrombotic or venous disease should be advised against prolonged periods of immobility during flight.

There is no apparent contraindication to air travel for the asthmatic subject if his condition can be controlled by medication and if oxygen is available. Passenger flying should not be considered advisable within ten days of receiving an artificial pneumothorax. The individual with suspected tuberculosis should be judged only on the basis of his infectivity to others, as passenger flying entails no undue hazard to his own health.

At least ten days should elapse after an abdominal operation before air flight is considered permissible, since expansion of intestinal gases at high altitudes could result in disruption of operative wounds, peritoneal soiling or other postoperative catastrophes.

Epileptic subjects prone to frequent seizures should travel with a companion, should receive adequate pre-flight medication and should have oxygen available during flight, since such persons appear to be more susceptible to seizures in aircraft.

Persons with sinusitis or otitis media should not fly during the acute stages of these infections.

Severe anemia or blood dyscrasias, in which the hemoglobin concentration is less than 8.5 g. %, impair the physiological response to even mild degrees of hypoxia. Patients with such disorders should be permitted to fly only if oxygen is immediately available throughout their flight. Since sickling and hemolysis may take place in persons with sickle cell disease, in the presence of mild to moderate deficiency of circulating oxygen, Negroes who contemplate passenger flying would be well advised to determine in advance whether or not they possess the sickle-cell trait, and to notify the flight attendant immediately should they experience any abdominal pain or discomfort. In such an event, the administration of oxygen tends to prevent further symptoms.

Patients with poliomyelitis are generally considered fit for air travel if one month has elapsed since the onset of their disease. Special arrangements are, of course, necessary for those who are not ambulant or who need a respirator.

Certain persons require careful study and assessment; and if they are permitted to fly on passenger aircraft, special handling. These include patients with mediastinal tumours, brain tumours, skull fractures, other conditions associated with increased intracranial pressure, spinal cord lesions, recent cerebrovascular accidents, large unsupported hernias, intestinal obstruction, angioneurotic edema with previous laryngeal involvement, multiple fractures, and persons in body casts. In general, casts affixed within 24 hours of flight should be bivalved to permit access during flight if necessary.

There is no contraindication to passenger flying for otherwise normal, healthy infants over six days of age, aged persons, pregnant women before the ninth month of gestation, or for controlled diabetics.

In actual fact there are but relatively few absolute contraindications to passenger air travel and these are based on common sense and an elementary understanding of atmospheric physics, physiological functions of the body, and the pathological features of the individual patient's disease.

Air travel has, indeed, been found to be the most expeditious and desirable form of transportation for patients with many types of illness, though some may need special preparation.

REFERENCES

1. Medical Criteria for Passenger Flying: A Joint Statement of the American Medical Association and the Aerospace Medical Association: *A.M.A. Arch. Environmental Health*, **2**: 124, 1961.
2. *Idem*: The Committee on Medical Criteria of the Aerospace Medical Association: *Aerospace Med.*, **32**: 369, 1961.

PREVENTION OF DISABILITY IN RHEUMATOID ARTHRITIS

TWO or three decades ago, the patient with rheumatoid arthritis was in danger of getting little or no treatment, of coming to understand that "nothing can be done". Hospital beds were seldom available; few well-equipped physical medicine departments existed; home physiotherapy care was virtually non-existent; rehabilitation programs were only concepts; and beyond "more rest and aspirin", treatment was only a long, demoralizing, passive, sanatorium-type regimen.

In the past ten years some of these deficiencies have been corrected. Today a greater danger faced by the patient with rheumatoid arthritis is that of bad treatment. Corticosteroid therapy has been recognized as hazardous by all who are experienced with its use by these patients. It may not be going too far to say that the presence of rheumatoid arthritis is now even considered by some to be a relative contraindication to the use of these drugs, as these patients who already suffer from a wasting, immobilizing disease, seem especially vulnerable

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to many of the side effects of the steroid hormones and their analogues. Yet such treatment is so easy to begin, so gratifying in the initial response, so well publicized to physicians and patients alike, that a high proportion of patients with arthritis are given a prescription for corticosteroids within the first few visits to their doctor.

What alternative therapy should be prescribed for these people, who have rested and taken salicylates and are growing increasingly desperate? The answer is a complex one, dull to read, poorly communicated in lectures. To try to answer this question and this need, a film has been produced, under the supervision of the National Medical Advisory Board of The Canadian Arthritis and Rheumatism Society. An approach to this problem arising in the treatment of rheumatoid patients has been described, the many details are presented with the force that only actual demonstrations can give, and many special techniques and procedures needed to deal with problem situations are illustrated. The film is distributed by The Canadian Arthritis and Rheumatism Society through its National Office, 900 Yonge Street, Toronto 5, or any of its eight Division Offices. H.A.S.

TO VICTORY OVER VODKA

THE reflections of a Soviet delegate to the 26th International Congress on Alcoholism held in Stockholm in July and August, 1960, provide reading material of considerable interest, particularly with regard to his contrast of the approach to public education in Russia with that employed by capitalist nations, and the lack of understanding in such countries of what he terms "the social roots" of alcoholism. (Sokolov, I. S., *Sovet. Zdravookhr.*, 2: 25, 1961).

This Russian observer comments on the number of presentations from the capitalist countries that reported an increasing prevalence of alcoholism particularly among the younger members of the population. How then, he asks, do the capitalist countries attempt to combat the abuse of alcohol? Of course, he observes, it would be hopeless to expect capitalists to possess any real understanding of the "social roots" of alcoholism. According to some capitalist teaching this affliction has its origin in inner conflict and the inability of the alcoholic to adapt to the demands and stresses of present-day society which lead to frustration and loss of perspective in private life. Others, he says, believe that the major cause of alcohol addiction is attributable simply to the euphoria-producing effect of this drug. In accord with such theories the capitalists' campaigns against this problem are channelled through various anti-alcohol leagues which are frequently supported by religious organizations such as the Canadian *Cercles Lacordaire* and treatment institutions such as *Les Maisons Domremy*. Various pamphlets, film strips and other types of information which are frequently cleverly designed with an attractive format are distributed to the public. Yet capitalist circles, the commentator notes, freely admit that all this propaganda has very little effect. Obviously, he states, this is inevitable because such measures fail to take into account the key fact that the social causes of alcoholism are rooted in present-day capitalist society. At the same time all of this propaganda against alcoholism is being countered by even more effective advertising by the purveyors of alcoholic beverages. Small wonder, then, that so many of the speakers at the Stockholm congress commented on the increasing prevalence of alcoholism despite the mounting tempo of anti-alcohol programs.

By contrast, we are informed that in the Soviet Union doctors look upon the alcoholic not as a sick person but as a morally unstable creature who requires, above all, re-education. Anti-alcoholism programs in Russia involve the co-operative efforts of complex teams of doctors, physiologists, biochemists, teachers, lawyers and workers in "cultural and hygienic educational institutes" with valuable assistance from the Red Cross and Red Crescent societies. Prophylactic measures are largely concerned with educational programs stressing repeated instruction on the damage that abuse of alcohol inflicts upon the organism.

In the U.S.S.R., regulations have been introduced to enforce absolute abstinence from alcohol by individuals engaged at industrial work or while driving a vehicle. Restrictions have been placed upon the sale of alcoholic beverages at various types of restaurants and eating places. At every public conference devoted to the promotion of health, the campaign against alcoholism is stressed and the degrading habit of drunkenness is deplored. The hazards of drinking while at work or while driving are dramatized by medical personnel in their public lectures on accident prevention. As a result of these measures, we are informed, there has been a gradual decrease in production and consumption of alcoholic beverages, particularly those of high alcohol content, in the Soviet Union.

In the socialist society, the social evils that promote alcoholism have been destroyed and such drunkenness as exists is the result of faulty upbringing, bad example, and decadent traditions and habits that are survivals from the past. This is the reason, according to our Soviet commentator, that in contrast to the hopeless outlook in capitalist countries, the Soviet propaganda campaign and mass movement against alcoholism, with the active participation of the nation's entire population, co-ordinated by government administrative decrees, have every hope for success.

To this decadent capitalist reader, all of the foregoing dialectic distils (you should forgive the expression) to the claim that alcoholism is being eradicated in Russia because the government decrees that it is a bad thing and forbids it.

LETTERS TO THE EDITOR

LYSOL

To the Editor:

I should like to draw attention to the use of the word "lysol" in my article in the March 11 issue of the *Canad. M. A. J.* (84: 549, 1961). The "lysol" referred to is that product listed in the British Pharmacopoeia as "Cresol and Soap Solution", "Liquor Cresolis Saponatus", "Liq. Cresolis Sap.", or "Lysol". This is not the same product as that manufactured by Lehn & Fink and marketed in Canada and the United States with the registered trade mark of "Lysol Brand Disinfectant". The latter contains no cresol, is not classed as a poison under any toxicity standard and owes its antibacterial activity to orthohydroxydiphenyl. The British Pharmacopoeia states that "The name LYSOL as a synonym for Cresol and Soap Solution may be used freely in many countries, including Great Britain and Northern Ireland, but in other countries exclusive proprietary rights in this name are claimed." The Dispensatory of the United States of America points out that "In parts of the British Empire where the word Lysol is a trademark, it may be used only when applied to the product made by the owners of the trademark."

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Ontario.

A DAY IN THE HOSPITAL

To the Editor:

With reference to "A Day in Hospital" mentioned in the London Letter (*Canad. M. A. J.*, 84: 1083, 1961) I hope that some, at any rate, of the suggestions put forward by British nurses will not be accepted in Canadian hospitals.

Having had considerable experience with hospitals in both countries, and in the latter also as a patient, I certainly condemn the early hour at which one is awakened. On the other hand I do not feel that it is expecting too much for patients to be clean and ready for examination, and the ward tidy, before the doctor arrives. Very often, after some patients have been well washed, certain physical signs not apparent under a layer of dirt manifest themselves, and at the same time, one would not be human if one did not carry out an examination more enthusiastically on some patients after they were clean. I well remember, whilst in practice in a Canadian city, at about 8 p.m. sending into hospital a dishevelled and dirty patient with a suspected coronary, but on visiting him at about 11 a.m. the following morning I still found him clad in his underwear and still filthy.

Neither do I feel that it is expecting too much for the ward to be cleaned before the doctor arrives, as apart from the noise and the inconvenience of having to avoid tripping over countless wires to which modern cleaning gadgets are connected, the patient is much happier, whilst being examined, at not having the ward cleaners hovering around the bed.

The morning temperature etc. of the patient may at times be irrelevant and the cause of unnecessary work for the nurse, but certainly recordings made the day before are of even less value.

Whilst appreciating that the nurse's lot could be improved, I would suggest that a salary increase would be more suitable than an alteration in her work, which could mean a deterioration in the service provided to the patient. I feel that in some respects we are already too slack and any acceptance in Canada of some of the British suggestions would be a retrograde step in the patient's care.

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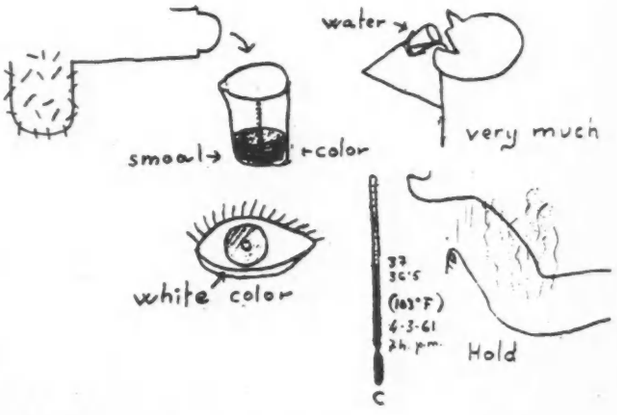
INTERPRETATION OF A PICTORIAL HISTORY

To the Editor:

I know that the articles published in the *Canadian Medical Association Journal* are of a high academic order. I sometimes wonder whether it wouldn't help life in these troubled times to insert something of a lighter intellectual thought. The following true story is an example of what I mean.

A Spanish seaman from a fishing ship came to my office accompanied by a male nurse and presented me with the pictorial history of his symptoms shown below.



The following was my interpretation. He is passing a small amount of dark-coloured urine. He was very thirsty and drank a lot of water. He had a high temperature. There was no evidence of jaundice. He had a very badly swollen, painful upper arm.

This may interest those who have had a similiar experience and prepare others who have not. On examination, the patient had an extensive cellulitis of the left arm with glands in the axilla. His left chest had a pleural effusion to the nipple line; on tapping, no organisms were obtained.

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MEDICAL NEWS IN BRIEF

ARTHRITIS: WHAT IS NEW AND IMPORTANT

In the October-December 1960 issue of *The Lahey Clinic Bulletin*, Fernandez-Herlihy has attempted, in simple and succinct terms, to indicate what is new and important in our knowledge of rheumatoid arthritis. The first landmark occurred when the disease was defined by Garrod in 1859 and the second in 1949 when cortisone was isolated and given with remarkable results to a patient with rheumatoid arthritis.

At present, the etiology remains unknown. The pleuropneumonia-like organisms (PPLO) have been investigated, but what they actually cause in animals is not arthritis but cellulitis. Although no organism has been successfully incriminated, many internists are impressed by the similarity between rheumatoid arthritis and an infection, even with regard to long-term sequelae, such as amyloidosis which occurs in from 20 to 30% of patients with rheumatoid arthritis. Genetic and immunologic factors are under most active study at the present time.

Pathologists have made it clear that rheumatoid arthritis is a systemic disease; the basic lesion seems to be a predominantly focal, vascular and connective tissue injury.

As to diagnosis, following the studies of Cecil (1930), Waaler (1940) and Rose (1948), in 1956 the first of the so-called latex fixation tests was developed. There are several variations of this test but the principle is the same in all. If a suspension of latex particles coated with gamma globulin is incubated with rheumatoid serum, agglutination visible to the naked eye will result in the majority of cases. None of the tests are completely specific, although most systems are highly sensitive. This phenomenon is due to the presence in rheumatoid serum of what is called rheumatoid factor. This factor is a gamma globulin of high molecular weight which has now been isolated in pure form and is being subjected to the closest scrutiny.

Although little progress has been made in the treatment of rheumatoid arthritis since cortisone was first used 12 years ago, the last decade has provided a new look at some old forms of treatment. The basic program of rest, heat and exercise, carefully tailored to the needs of the individual patient, is the best form of management available. It is one to which other forms of treatment, if they become necessary, can be added, and without which the drug therapy of rheumatoid arthritis is generally useless.

Ever since gold treatment was introduced more than 30 years ago, the question of its efficacy in rheumatoid arthritis has gone unanswered. Rheumatologists have been divided into gilders and nongilders and their degree of enthusiasm for the use of gold seemed to be dependent only upon the frequency with which they used it. Recently, the results of a long-term, controlled, double-blind study of gold therapy in a large group of rheumatoid patients showed statistically significant results (*Ann. Rheumat. Dis.*, 19: 95, 1960), but the permanence of the improvement still remains to be shown. Rheumatoid patients have also been treated by small, daily self-administered doses of ACTH (taken in much the same way as the diabetic takes insulin), the one advantage is that there is no problem of adrenal suppression.

The author does not consider the use of nitrogen mustard in "malignant" rheumatoid arthritis or, on the basis of his own wide experience, antimalarial drugs, of any particular value; he fails to comment on phenylbutazone therapy. In his concluding remarks, he states that he envisions three approaches to the final goal: first, conservatism in the current management of rheumatoid arthritis; second, a more aggressive attitude toward the rehabilitation of the arthritic, and third, continued and accelerated inquiry into the fundamental process of this disease.

IMMUNOLOGICAL ASPECTS OF RHEUMATIC FEVER AND RHEUMATOID ARTHRITIS

Rheumatic fever and rheumatoid arthritis have long been thought of as being in some way related. The lesions in the two diseases are morphologically similar in certain respects and it has been argued by analogy with experimental results that they represent hypersensitivity reactions. Today it is a widely held and reasonably substantiated hypothesis that the pathologic mechanism in both involves some form of immunological response, leading through abnormal tissue reactivity to sterile granulomatous lesions in the connective tissues. Such a response implies the presence of a provocative antigen. In rheumatic fever, *Streptococcus pyogenes* is the source of this antigen. Although rheumatic fever has now come largely under control through the use of hygienic measures and therapeutic agents effective against the streptococcus, nothing is really understood about the mechanism of the disease (Leading Article, *Brit. M. J.*, 1: 565, 1961).

Rheumatoid arthritis is an even greater problem: methods of prevention are unknown; treatments offer only alleviation, not cure; and the causative agent of the disease is as obscure as its pathological mechanism. Investigations indicate that autoimmune phenomena are probably of significance in the pathogenesis of rheumatoid disease. The vascular and subcutaneous lesions are similar to those induced experimentally by immunological procedures, and are usually populated with plasma cells. The newer work with serological reactions, especially with the rheumatoid factor, suggests that the factor is an antibody capable of reacting with potential antigens in the patient. The rheumatoid factor is a gamma globulin with a large molecule and a sedimentation coefficient of 19S. It has been detected in the cytoplasm of plasma cells at various stages of maturity in the synovial tissues, lymph nodes and occasionally the nodules of patients with rheumatoid arthritis.

Several suggestions have been made as to the identity of the antigen to which the rheumatoid factor is an antibody, if, indeed, it is an antibody. Chemical and physical changes in gamma globulin may frequently occur and may supply the antigen to which the factor relates, but there is no proof that such an autoimmune mechanism plays any part in the causation of the disease. The pattern of tissue reaction in chronic rheumatism resembles the delayed or tuberculin-type of

hypersensitivity reaction and is therefore probably independent of the presence of circulating antibodies. Supporting this view is the observation that rheumatoid arthritis has often occurred in patients with agammaglobulinemia.

These various immunological phenomena are rarely observed in healthy persons, but how any of them could have a role in the origin and maintenance of rheumatoid arthritis needs, as yet, to be explained.

MAMMARY SOUFFLE

To the differential diagnosis of cardiac murmurs heard during pregnancy and lactation must be added the so-called mammary souffle of pregnancy and lactation (Annotation: *Brit. M. J.*, 1: 806, 1961).

This murmur may occur during second and third trimesters of pregnancy and during lactation; it does not occur during the first trimester. It is heard in the second intercostal spaces most frequently, but may be heard in the third and fourth left intercostal spaces. There is an interval between the first heart sound and the onset of the murmur. The timing may be solely systolic or it may continue into or throughout diastole. It is of high frequency and is heard best with the patient lying flat. It radiates only poorly and is eliminated by lateral compression in the corresponding intercostal space. It is associated with a prominent intercostal pulsation near the site of the murmur.

This murmur is believed to be due to changes in hemodynamics such that blood is preferentially diverted towards the breasts during pregnancy and lactation.

The importance of the mammary souffle lies in its recognition and the frequency with which it occurs.

HUMAN HAIR LOSS

The pathologic dynamics of hair loss in humans are discussed in detail in a report by Kligman (*A.M.A. Arch. Dermat.*, 83: 175, 1961). The author first defines his terms. Catagen is that brief period during which a growing follicle (anagen) becomes transformed into a resting one (telogen). When a hair follicle becomes "harassed" or "insulted" it reacts by going into telogen. When these telogen hairs fall out they present clinically as club hairs. The author calls excessive loss of club hairs "telogen effluvium". As a practical working figure telogen (or club hair) counts higher than 25% are diagnostic of telogen effluvium. The telogen count in the usual clinical instance of telogen effluvium rarely exceeds 50%. Only the scalp was studied because it is much more susceptible to hair loss.

Six causes of telogen effluvium are discussed in detail.

1. Postfebrile telogen effluvium following typhoid fever, scarlet fever, pneumonia, etc., is well known. The hair loss begins within two to three months of the febrile episode. Regeneration is well under way within six weeks after excessive shedding stops.

2. Postpartum telogen effluvium begins two to four months after parturition. Usually shedding continues for two to five months although occasionally it may last up to one year. Restitution is complete unless some other process intervenes. If the patient develops female pattern baldness (akin to male pattern baldness) immediately after postpartum effluvium, then she may falsely assume that her permanent hair loss was related to her pregnancy.

3. Psychogenic telogen effluvium or idiopathic telogen effluvium is a poorly defined entity occurring more commonly in women and having telogen (club hair) counts of doubtful significance.

4. Chronic systemic disease with great wasting (such as terminal carcinoma, leukemia and tuberculosis) also produces telogen effluvium. In such cases, it was noted that the degree of hair loss was proportional to the degree of wasting.

5. Telogen effluvium of the newborn is a condition which is probably physiological. It occurs from birth up to four months. Telogen counts up to 87% were found, indicating that there is a more or less synchronized replacement.

6. Heparin telogen effluvium occurs usually after a latent period of three months. If not too severe, manifest alopecia may not occur.

The author then proceeds to certain other aspects of this condition. As a general rule the follicle responds in an all-or-none fashion (i.e. it either produces a club hair or it doesn't). Cancer chemotherapeutic agents stop the reproduction of hair matrix cells and produce an anagen effluvium. This type of hair loss begins in a week or so, while telogen effluvium has a latent period of months. Assuming that there are 100,000 hairs on the average scalp, at least 25% or 25,000 hairs must be shed before unmistakable thinning develops. An average daily loss of 100 hairs or more is probably abnormal. With telogen effluvium the loss of the hair is a sure sign of its restoration. When the physician satisfies himself that only club hairs are being lost from the normal scalp, he can confidently predict replacement of every hair. Diagnosis of telogen effluvium is made by determining the percentage of telogen hairs on the scalp and by counting the number of club hairs shed each day.

This condition is obviously a non-specific reaction pattern provoked by a host of different stimuli—a syndrome, not a disease. It has only the barest qualifications as a pathologic state in that it merely represents a shortening of the follicle's life expectation.

SUDDEN DEATH FROM CORONARY DISEASE

Five hundred consecutive sudden deaths ascribed to coronary arteriosclerotic heart disease after complete autopsy were studied by Adelson and Hoffman (*J. A. M. A.*, 176: 129, 1961), with special attention to coronary vessels and myocardium. In 184 cases, new disease (recent thrombosis, acute myocardial infarct, or both) explained the sudden catastrophe. The remaining cases presented only chronic degenerative coronary disease, frequently associated with healed infarcts.

The authors believe that the cardiac mechanisms responsible for sudden death in coronary disease must of necessity differ in these two groups with such disparate morbid anatomy. The presence of an intact myocardium in many of these patients suggests that the potentiality for good cardiac function exists if the heart beat can be restored. Such positive measures as intermittent rhythmic manual compression ("cardiac massage"), electrical defibrillation, or both in association with artificial respiration are indicated when the physician is present at a death occurring under these circumstances.

(Continued on advertising page 25)

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MEDICAL MEETINGS

MONTREAL PHYSIOLOGICAL SOCIETY

The Montreal Physiological Society held its annual business meeting at the Ayerst Research Laboratories on May 8, 1961. Three new members of the Society were elected — Dr. Mimi Belmonte, Mrs. Norah Hildebrand and Dr. Daya Ram Varma. A new executive for the 1961-62 season was elected by acclamation: President, Dr. Edouard Pagé; Vice-President, Dr. Donald Fairbairn; Secretary, Dr. J. M. Parker. The new members to serve on the executive committee for a two-year term are Dr. D. V. Bates, Dr. J. P. Cordeau and Dr. C. Von Seeman. The retiring president, Dr. Eleanor R. Harpur, in her presidential address spoke on the subject of "Clinical Chemistry". Dr. Harpur spoke of the clinical chemist from the viewpoint of her own work as Head of Biochemistry at the Montreal Children's Hospital. The clinical chemist varies markedly from place to place, depending on personality, training and work, and may range in background from that of a doctor of medicine with a yen for investigation to that of a fully trained Ph.D. in chemistry. At the Montreal Children's Hospital, one of the unique problems was to develop "ultramicro" techniques suitable for work with the small amounts of blood available from an infant. Dr. Harpur pointed out that "macro" techniques require 1 or more ml. of fluid, "micro" techniques 0.1 to 1 ml. and "ultra-micro" methods less than 0.1 ml. of blood or fluid. The latter techniques require special glassware and pipettes that are accurate and easy to use. Fortunately these have become available in the last few years. This has been one of their secrets of success. Another is special adaptation of instruments such as the spectrophotometer by reduction of the height and width of the curvette without any sacrifice in the length of the light path. In addition to the technical difficulties, the number of tests available has greatly increased over the last five years. For instance, a baby brought in to hospital suffering from diarrhea and dehydration may have determinations of hematocrit, sodium and potassium, blood pH, bicarbonate and chloride instead of the single CO_2 combining power requested in former years. At the Montreal Children's Hospital it is possible to perform all of these estimations on three capillary tubes of blood. Dr. Harpur then spoke of special tests more directly related to the research interests of the hospital such as determinations of various enzyme activities. As examples she discussed the chemical procedures involved in studies of glycogen storage disease and metabolic disorders such as galactosemia. In the latter the diagnosis can be confirmed by the absence of galactose-1-phosphate uridyl transferase in the red blood cells. The Montreal Children's Hospital functions as a poison control centre for the English-speaking population of the Province of Quebec, and many biochemical tests are required in the diagnosis and management of poisonings. There are approximately five to 10 calls or visits to the hospital for poison cases daily, of which 25% are salicylate poisonings, usually due to ingestion of flavoured forms of acetylsalicylic acid. The hospital has found that, as a general rule, if less than one grain of salicylate per pound of body weight has been ingested, the prognosis is good; if the quantity ingested exceeds this level, the patnent is admitted for observation and treatment. The next commonest type of poisoning is due to hydrocarbons, and as these chemicals are excreted via the lungs their ingestion is often complicated by pneumonia. Blood levels of barbiturates are carried out on patients with barbiturate intoxications. When exchange transfusions are necessary in various types of poisonings, biochemical monitoring is essential. Another function of the biochemical laboratory of the Children's Hospital is to provide assistance to various research programs, such as those concerned with the study of cystic fibrosis of the pancreas. Here the investigators are engaged in determining the serum protein patterns of patients and their relatives, and have demonstrated an abnormal serum component which may ultimately identify the heterozygote carriers. Studies with a pump oxygenator relating to ways and means of increasing the duration for which this equipment can be used safely have been greatly assisted by biochemical measurements. Liver function studies in the newborn are other problems requiring chemical methods adapted on a "micro" scale. Dr. Harpur showed conclusively how an active and expanding department of clinical chemistry can enlighten diagnostic difficulties and be of aid in treatment regimens throughout the hospital.

J. M. PARKER, M.D.,
Secretary.

ASSOCIATION NOTES

SCHOOLS APPROVED BY THE C.M.A. FOR THE TRAINING OF RADIOLOGISTS IN CANADA

The following is the first complete list of schools approved by the Canadian Medical Association for training radiological technicians in Canada.

At the request of the Canadian Association of Radiologists and the Canadian Society of Radiological Technicians, in June 1959 the General Council of the C.M.A. accepted the responsibility of approving schools for training radiological technicians. Since that time, the C.M.A. Committee on Approval of Schools for Training Radiological Technicians has prepared a revised set of standards and application forms, and has reviewed all of the schools which had previously received "interim" approval by the Joint Council on Technical Training of C.A.R. and C.S.R.T. This list comprises those schools that have been approved following the reappraisal that has gone on during the past two years.

SCHOOLS APPROVED FOR TRAINING RADIOLOGICAL TECHNICIANS IN DIAGNOSTIC TECHNIQUE BY THE C.M.A. COMMITTEE ON APPROVAL OF SCHOOLS FOR TRAINING RADIOLOGICAL TECHNICIANS

School or hospital	*City*	*Beds*	*Students taken Yearly*	*Students taken Total*	*Director*
British Columbia					
Royal Columbian Hospital	New Westminster	500	6	12	R. E. Mitchell*
North Vancouver General Hospital	Vancouver	142	2	3	A. Paramonoff
St. Paul's Hospital	Vancouver	600	10	12	John S. Madill
Shaughnessy Hospital, D.V.A.	Vancouver	1152	2	2	Andrew Turnbull
Vancouver General Hospital	Vancouver	1600	8	16	R. W. Boyd
Royal Jubilee Hospital	Victoria	504	4	8	H. M. Edmison
St. Joseph's Hospital	Victoria	500	6	12	Frank G. Stuart
Alberta:					
Calgary General Hospital	Calgary	732	5	9	K. D. Symington
Drs. Hall and Windle	Edmonton	—	1	2	S. C. Windle
Edmonton General Hospital	Edmonton	441	5	11	R. M. Clare
Misericordia Hospital	Edmonton	425	4	9	M. Mallett
Royal Alexandra Hospital	Edmonton	884	6	14	C. F. Hyndman
University Hospital	Edmonton	1250	4-5	9	H. E. Duggan
Lethbridge Municipal Hospital	Lethbridge	192		7	M. M. Marshall
St. Michael's Hospital	Lethbridge	183	2	4	Brian O. Black
Parsons Clinic	Red Deer	150	2	4	W. B. Parsons
Saskatchewan:					
Moose Jaw Union Hospital	Moose Jaw	245	1	2	N. Elliott Dunn
Providence Hospital	Moose Jaw	164	1	2	H. O'Rielley
Victoria Union Hospital	Prince Albert	180	2	5	Thomas J. Ho
Holy Family Hospital	Prince Albert	133	2	4	Thomas J. Ho
Medical Arts Clinic	Regina	—	3	6-9	H. P. Kent
Regina General Hospital	Regina	940	4-5	12	A. J. Richards
St. Paul's Hospital	Saskatoon	282	2	4	A. Becker
University Hospital	Saskatoon	525	4	8	E. W. Spencer
Manitoba:					
Brandon General Hospital	Brandon	160	1	2	R. H. D. Sykes
Manitoba Government School	Portage la Prairie	89	11	35	A. W. McCullough
St. Boniface Hospital	St. Boniface	700	8	16	C. W. Hall
Deer Lodge Hospital, D.V.A.	St. James	715	1-2	3	T. W. Hayter
Grace Hospital	Winnipeg	290	3	6	G. W. Ritchie
Misericordia Hospital	Winnipeg	427	9	9	E. Gedgaudas
Winnipeg Children's Hospital	Winnipeg	232	2	4	A. E. Childe
Winnipeg General Hospital	Winnipeg	862	8	16	R. A. Macpherson
Ontario:					
Belleville General Hospital	Belleville	220	2	4	Peter G. Loder
Brantford General Hospital	Brantford	545	4	6-8	W. E. Crysler
St. Joseph's Hospital	Brantford	168	2	3	J. M. Willinsky
St. Joseph's Hospital	Chatham	211	1	2	J. L. Callaghan
McKellar General Hospital	Fort William	426	4-5	7	A. Molle
South Waterloo Memorial Hospital	Galt	220	3	6	W. R. Bell
Hamilton General Hospital	Hamilton	1100	4	8	T. W. Dean
McGregor Clinic	Hamilton	—	1	3	J. G. Stapleton
Hôtel-Dieu Hospital	Kingston	320	3-4	8	Bruce T. Colwell
Kingston General Hospital	Kingston	513	8	16	S. L. Fransman
Kirkland and District Hospital	Kirkland Lake	160	1	2	K. C. H. Middlemiss
Kitchener-Waterloo Hospital	Kitchener	440	5	8	M. B. George
Ross Memorial Hospital	Lindsay	140	1	2	D. C. Pitt
St. Joseph's Hospital	London	437	7	14	M. B. Hill
Victoria Hospital	London	900	6	12	G. G. Copestake
Greater Niagara General Hospital	Niagara Falls	309	3	6	Margaret E. Bickle
North Bay Civic Hospital	North Bay	100	1	2	T. A. M. Thompson
St. Joseph's General Hospital	North Bay	200	2	5	T. A. M. Thompson
Orillia Soldiers' Memorial	Orillia	120	1	2	T. M. McLennan
Ottawa Civic Hospital	Ottawa	900	6-9	20	T. G. Stoddart
Ottawa General Hospital	Ottawa	622	6	12	Conway Don
St-Louis-Marie de Montfort Hospital	Ottawa	216	2	4	J. A. E. Tessier
St. Joseph's Hospital	Peterborough	169	2	5	K. W. Milne
General Hospital of Port Arthur	Port Arthur	282	2	4	W. A. Hargan
St. Joseph's Hospital	Port Arthur	220	2	4	W. A. Hargan
St. Catharines General Hospital	St. Catharines	400	7	12	G. T. Zumstein
St. Thomas-Elgin General Hospital	St. Thomas	378	1	2	W. B. Taylor
St. Joseph's Hospital	Sarnia	345	5	7	
Sarnia General Hospital	Sarnia	247	2	5	G. R. Scarrow
Sudbury Hospitals (3 hospitals)	Sudbury	750	4-6	12	C. L. Crang
St. Joseph's Hospital	Toronto	700	4-5	10	Wallace M. Roy
St. Michael's Hospital	Toronto	950	6	12	E. H. Shannon
Toronto East General and Orthopedic	Toronto	750	4	8	A. R. McGee
Toronto General Hospital	Toronto	1500	4-8	13	D. E. Sanders
Toronto Western Hospital	Toronto	700	3	7	L. R. Harnick
Welland County General Hospital	Welland	251	1	2	Donald MacNeill

*Every Director is an M.D. certificated in Radiology or holds equivalent qualifications.

School or Hospital	City	Beds	Students taken Yearly	Students taken Total	Director
Ontario—continued:					
Humber Memorial Hospital	Weston	120	2	4	J. M. Dunsmore
Hôtel-Dieu of St. Joseph	Windsor	390	2	3	N. L. Hillary
Quebec:					
Hôpital Ste-Croix	Drummondville	180	3	6	Gaston Rodrigue
Hôpital du Sacré-Cœur	Hull	320	2	4	Henri Charette
Associated Hospitals of Montreal School of Radiography			7-8	14	Arthur D. French
Queen Elizabeth Hospital		275			E. M. Crawford
Jewish General Hospital		384			Isadore Sedlezky
Reddy Memorial Hospital		139			G. P. Larini
St. Mary's Hospital		347			J. C. Lanthier
Montreal Children's Hospital		300			J. Scott Dunbar
Hôpital Ste-Justine	Montreal	860	5-7	15	Marc del Vecchio
Hôpital Maisonneuve	Montreal	467	6	10	Jules Laberge
Hôpital Saint-Luc	Montreal	414	4	8	Ls. Ivan Vallée
Hôtel-Dieu de Montréal	Montreal	750	6-8	15	Albert Jutras
Montreal General Hospital	Montreal	751	8-9	18	D. J. Sieniewicz
Notre-Dame Hospital	Montreal	865		20	Yvan Methot
Royal Victoria Hospital	Montreal	1017	6-8	16	C. B. Peirce
Sacred Heart Hospital	Montreal	800	4-6	12	O. Raymond
Hôpital Ste-Jeanne-d'Arc	Montreal	479	4-8	12	A. F. Vallée
Hôpital de l'Enfant-Jésus	Quebec	607	2	6	Henri Lapointe
Hôpital St-François d'Assise	Quebec	400	2-3	6	J. C. Robitaille
Hôpital du Saint-Sacrement	Quebec	500	2	3	Luc Audet
Hôpital Général St-Vincent-de-Paul	Sherbrooke	275	5	10	R. L. Duberger
Hôtel-Dieu de Sherbrooke	Sherbrooke	400	4	6	André d'Etchévery
Sherbrooke Hospital	Sherbrooke	150	2	2	John Silny
New Brunswick:					
Hôtel-Dieu de St-Joseph	Campbellton	201	1	1	F. St. Laurent
Victoria Public Hospital	Fredericton	227	2	4	A. M. Edington
Moncton Hospital	Moncton	298	3	6	H. R. Ripley
Saint John General Hospital	Saint John	500	8	16	N. S. Skinner
Saint Joseph's Hospital	Saint John	254	3-5	10	E. A. Petrie
Nova Scotia:					
Canadian Forces Hospital	Halifax	174		6	(Surg. Cmdr.) W. M. Little
Affiliated with Canadian Forces Hospitals at Kingston and Rockcliffe, and H.M.C.S. *Naden*, Esquimalt, British Columbia					
Halifax Infirmary	Halifax	223	6-8	13	Charles M. Jones
St. Rita's Hospital	Sydney	162	3-4	6	H. R. Corbett
Sydney City Hospital	Sydney	233	3	6	H. R. Corbett
Prince Edward Island					
Charlottetown Hospital	Charlottetown, P.E.I.	188	1-2	3	W. L. MacDonald
Prince Edward Island Hospital	Charlottetown, P.E.I.	245	1-2	3	W. L. MacDonald
Newfoundland:					
St. John's General Hospital	St. John's	456	10	20	H. B. Murphy

SCHOOLS APPROVED FOR TRAINING RADIOLOGICAL TECHNICIANS IN THERAPEUTIC TECHNIQUE

British Columbia Cancer Institute, Vancouver General Hospital	Vancouver	56* 20	2	3	A. Maxwell Evans
Saskatoon Cancer Clinic University Hospital	Saskatoon	500	1	4	T. A. Watson
Manitoba Cancer Treatment and Research Foundation	Winnipeg		3	6	R. J. Walton
Winnipeg General Hospital		862			
St. Boniface Hospital		700			
Ontario Cancer Foundation, Hamilton Clinic Hamilton General Hospital	Hamilton	25	1	2	L. S. Green
Ontario Cancer Foundation, Kingston Clinic Kingston General Hospital	Kingston	513	1	2	R. C. Burr
Hôtel-Dieu Hospital		320			
Ontario Cancer Foundation, Ottawa Clinic Ottawa Civic Hospital	Ottawa	36	1-2	3	T. C. Stoddart
Ottawa General Hospital		692			
Ontario Cancer Institute Princess Margaret Hospital	Toronto	137	2-1 yr. course 4-2 yr. course	12	C. L. Ash
Montreal General Hospital	Montreal	751			D. J. Sieniewicz
Notre-Dame Hospital	Montreal	865		4	Yvan Methot
Royal Victoria Hospital	Montreal	1017	2	2	Carleton B. Pierce Jean Bouchard
Saint John General Hospital	Saint John	600	1-2	1-2	John A. Caskey
Victoria General Hospital	Halifax	556	2	4	J. E. Stapleton

*In some cases total hospital capacity is given and in others that used for therapy only.

INFORMATION FOR CANADIAN DOCTORS ON

FINANCIAL ASSISTANCE AVAILABLE FOR GRADUATE OR POSTGRADUATE MEDICAL STUDY

in

CANADA - UNITED STATES - EUROPE

(PART 6*)

Through its Journal, The Canadian Medical Association is pleased to provide up-to-date information on financial assistance that is available to facilitate the graduate and/or postgraduate medical education of Canadian doctors. Owing to space limitations, we are not in a position to publish the complete list of medical award classifications at this time. Please refer to other issues of the Journal, if the subject in which you are interested is not listed herein.

Unless otherwise indicated, the value of the awards will be quoted in the currency of the country mentioned. As entry regulations into a foreign country vary, it is recommended that the applicant for postgraduate study first investigate all details through the Embassies of the foreign countries concerned. Applicants should satisfy themselves whether medical registration in the jurisdiction of the award is or is not a requirement to hold the postgraduate post in the country selected.

In so far as entry into the United States is concerned, simply communicate with the U.S. consular office nearest your place of residence. These offices are located in the following cities: St. John's, Newfoundland; Halifax, Nova Scotia; Saint John, New Brunswick; Quebec, Quebec; Montreal, Quebec; Ottawa, Ontario; Toronto, Ontario; Windsor, Ontario; Winnipeg, Manitoba; Calgary, Alberta; Edmonton, Alberta; and Vancouver, British Columbia.

It is understood that a Canadian citizen entering the United Kingdom must have a valid passport but that no visa is necessary. Application forms for passports can be obtained at any large Canadian Post Office and should be completed and sent to the Chief Passport Officer, Ottawa, Ontario.

Name of Award	Field of Study	Where Tenable	Value	Number Available	Duration	Conditions	Apply to
OPHTHALMOLOGY — UNRESTRICTED							
Alexander Pigott Wernher Memorial Travel Fellowships	Ophthalmology, otology	Unrestricted	£900 per annum if married, or £650 if single (subject to adjustment in case of fellowships tenable outside the sterling area), plus transportation, tuition, laboratory materials	Unspecified	One year	Available to nationals of the United Kingdom and British Empire; must have a medical qualification and research experience in ophthalmology or otology. Awards are for specific research toward the prevention and cure of blindness and deafness	The Secretary, Medical Research Council, 38 Old Queen Street, Westminster, London, S.W.1, England, by October 31
ORTHOPEDIC SURGERY — UNITED KINGDOM							
Canadian Orthopædic Association: Exchange Fellowship	Orthopedic surgery	United Kingdom	$500	One, every two years	Six weeks	Candidate must not be over 40; must have Canadian Fellowship in orthopedic surgery or an equivalent qualification	Dr. R. I. Harris, Chairman of the Committee on Exchange Fellowships, Canadian Orthopædic Association, 609 Medical Arts Bldg., Toronto 5, Ont.
ORTHOPEDIC SURGERY — UNRESTRICTED							
Robert Jones Travelling Research Scholarship	Orthopedic surgery	Unrestricted	£500	One, every four years; next available in 1962	One year	Available to nationals of all countries; must be qualified surgeons	The Secretary, Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2, England
OTOLARYNGOLOGY — CANADA							
University of Toronto O'Keefe Fellowships	Postgraduate study or research in otolaryngology	University of Toronto	Up to $1800 per annum	Unspecified	One year	Awarded to graduates in medicine on recommendation of Head, Department of Otolaryngology	Professor of Otolaryngology, Faculty of Medicine, University of Toronto, Toronto 5, Ont.

*See also page 1038, May-6; page 1092, May 13; page 1148, May 20; page 1214, May 27; page 1397, June 17.

Name of Award	Field of Study	Where Tenable	Value	Number Available	Duration	Conditions	Apply to
OTORHINOLARYNGOLOGY — UNITED KINGDOM							
Geoffrey E. Duveen Studentship		University of London	£700	Not known what intervals award will be available	Unspecified	Available to nationals of all countries for research; must be registered practitioners, or have had appropriate previous education and experience	The Academic Registrar, University of London, Senate House, London, W.C.1, England
OTOLOGY — UNRESTRICTED							
American Otological Society, Inc. Research Fund	Otosclerosis	Unspecified	Value dependent on study planned and determined by the Trustees	Unspecified	Unspecified	Open to nationals of any country	Dr. Philip E. Meltzer, Secretary, The Central Bureau of Research, American Otological Society Inc., 285 Commonwealth Ave., Boston 16, Mass.
PEDIATRICS — CANADA							
University of Toronto: Elizabeth Arbuthnot Dyson Fellowship	Research in pediatrics	University of Toronto	Annual income from $25,000	One annually, if income sufficient	One year	Open to graduates in medicine from any approved university. Award made on recommendation of the Head, Department of Pediatrics	Professor of Pediatrics, Faculty of Medicine, University of Toronto, Toronto 5, Ont.
PEDIATRICS — UNITED KINGDOM							
Cambridge University: Gwynaeth Pretty Research Studentship	Research in the etiology, pathology or treatment of disease with particular, but not exclusive reference to diseases which cripple or disable in childhood or early life	Cambridge University	£250	One	Three years; in **exceptional** cases, renewable for a further period	Open to graduates of any university. If student not a member of Cambridge University, must become one	Professor of Pathology, Department of Pathology, Tennis Court Road, Cambridge, England
Manchester University: Ashby Memorial Research Scholarship	Pediatrics	University of Manchester	Unspecified	One every 3 years; next offer 1961	One year (renewable)	Open to any medical practitioner registrable in England	The Registrar, University of Manchester, Oxford Road, Manchester, England, before July 1
PEDIATRICS — UNRESTRICTED							
International Children's Centre	Social pediatrics	France and abroad	Covers maintenance, travel expenses during the course, tuition, pocket money. Transportation shall be paid by the government of the participant or by the participant himself	Twenty-five	Three months (April to July)	Open to doctors, pediatricians and public health officials responsible for maternity and child welfare services. Course is intended primarily for doctors who are responsible for the programs organized jointly by UNICEF and the governments of various countries	Education Department of the International Children's Centre, or Ministry of Health in candidate's own country
Queen Elizabeth II Canadian Fund to Aid in Research on the Diseases of Children Fellowships	Research related to diseases of children	Unrestricted subject to approval	$3500 to $5000 per annum	Variable	One year (renewable)	Available to Canadian citizens or residents who have graduated with high standing from approved medical school university with M.D. or Ph.D. degree. Candidates must not be over 35 years of age	Board of Trustees, Queen Elizabeth II Canadian Research Fund, c/o National Research Building, Ottawa 2, by January 15
PATHOLOGY — CANADA							
University of Toronto: Graham Campbell Fellowship	Pathology	Department of Pathology, University of Toronto	Interest on $5000	One	One year (renewable)	Open to graduates in medicine of the University of Toronto	Professor of Pathology, Faculty of Medicine, University of Toronto, Toronto 5, Ont.
PATHOLOGY — UNITED KINGDOM							
Queen's University (Belfast): John Dunville Fellowship		Queen's University	£500	One	Three years	Open to persons either of whose parents was born, or who for at least 20 years resided in Great Britain or Northern Ireland. Object of the Fellowship: (a) to educate the Fellow in pathology and medical science; (b) to enable him to qualify for academic and	The Dean, Faculty of Medicine, Queen's University, Belfast, Northern Ireland

Name of Award	Field of Study	Where Tenable	Value	Number Available	Duration	Conditions	Apply to
PATHOLOGY — UNITED KINGDOM							
						other medical appointments; (c) to enable the Fellow to engage in experimental pathology; (d) to advance knowledge in pathology and medicine	
Charles Graham Medical Research Fund		University of London	£400 per annum	Not known at what intervals the award will be available	Two years	Available to nationals of all countries for research; award to enable recipient to continue pathological research; and at the same time to secure his services to the School of Advanced Medical Studies connected with University College Hospital as a teacher, under the direction of a professor of pathology	The Academic Registrar, University of London, Senate House, London, W.C.1, England
London University: Charles Graham Medical Research Fund		London University	£400 per annum	One	Two years, awarded from time to time	Scholar is required to undertake teaching as well as research work	Academic Registrar, London University, London, England
London University: John Marshall Fellowship	Surgical pathology	University College Medical School in Graham Research Department	£700 per annum, with superannuation benefits	One	Two years (renewable for third)	Awarded by University on nomination of Medical School	The Dean, University College Hospital Medical School, University of London, London, England
Oxford University: Philip Walker Studentship	Research in pathology	Oxford University	Not less than £200 per annum	One	Up to five years	Open to graduates of any university; must be qualified to undertake original research in pathology	The Registrar, University Registry, University of Oxford, Oxford, England
Musgrave Research Studentship	Pathology	Queen's University, Belfast	£650 per annum	One approx. every two years; next available 1961-62	One year (renewable)	Available to British subjects; must be graduates of at least one year's standing of a university in the British Commonwealth, who are engaged in or show marked capacity for original research in pathology	The Secretary, Queen's University, Belfast, Northern Ireland, by June 1
Liverpool University: Thelwall Thomas University Scholarship	Surgical pathology	Liverpool University	£400 per annum	One	One year (renewable for a second)	Open to graduates of any university should a suitable candidate of Liverpool University not be forthcoming	The Dean, Faculty of Medicine, University of Liverpool, Liverpool 3, England
Cambridge University: John Lucas Walker Studentship	Original research in pathology	Cambridge, for at least three terms of tenure	Not exceeding £500 per annum	One, not exceeding £500 per annum, **possibly** a second, not exceeding £400 p. a.	Three years (in **exceptional** cases renewable for a further two years)	Open candidature, but students must become members of Cambridge University	Professor of Pathology, Department of Pathology, Tennis Court Road, Cambridge, England
PATHOLOGY — UNRESTRICTED							
University of Toronto: Helen L. Vanderveer Fellowship	Pathology	An approved university	Income from $50,000	One	One year	Graduate in medicine of an approved university for postgraduate study and research in pathology	Professor of Medicine, University of Toronto, Toronto 5, Ont.
George Christian Hoffman Alpha Fellowship	Pathology	Europe or United States	Approx. $915	One	One year	Open to recent graduates of Queen's University. Awards will be made on the basis of composite standing in the last three years of the course leading to the M.D. degree	Secretary, Faculty of Medicine, Queen's University, Kingston, Ont., by March 1

(To be continued)

AMENDMENT TO PREVIOUS LISTING

The listing of the R. Samuel McLaughlin Foundation: Travelling Fellowships, published in *Canad. M. A. J.*, 84: 1096 (May 13), 1961, should be amended as follows:

Field of Study: Clinical science.

Where Tenable: Some medical centre other than the candidate's own.

Value: $250 per month, plus extra allowance for dependants, and transportation costs.

Canad. M. A. J.
June 24, 1961, vol. 84

OBITUARIES

DR. DAVID H. BODDINGTON, 80, died May 3 in Sunnybrook Hospital, Toronto. Born in Sparta, Ont., Dr. Boddington graduated from the University of Toronto Medical School in 1905 and served on the teaching staff of St. Michael's and St. John's Hospitals. He retired from general practice in 1959 after practising in Toronto for more than 50 years.

In World War II he served with the Royal Canadian Army Medical Corps overseas, and in China and Russia. He was a life member of the Toronto Academy of Medicine and Faculty Union of the University of Toronto.

He is survived by his widow and three sons. One, Dr. George Boddington, practises in Toronto.

DR. JOHN M. H. GILLIES, 89, died April 20 at Teeswater, Ont., where he had lived in retirement after serving the local community as medical adviser for over 50 years.

DR. ALBERT HAZELL, 58, died April 27 in Saskatoon. An honour student in medicine, Dr. Hazell graduated from the University of Toronto Medical School in 1928. He served his internship at the Winnipeg General Hospital and took a postgraduate course in internal medicine at the University of Saskatchewan, where he later became an instructor in clinical medicine. Ill health forced him to retire from general practice in 1934.

Dr. Hazell is survived by his widow and two sons.

CHARLES HUDSON LEAVENS, M.D., C.M., E.D., C.D., died suddenly at his home in Port Hope, Ont., on March 19, 1961.

Dr. Leavens was the son of the late Mr. and Mrs. Charles C. Leavens of Belleville. He was educated at the Belleville Collegiate and Business School and graduated from Queen's University Medical School in 1935. He was engaged in general practice in Picton, Ont., from 1935 until 1939. He joined the Hastings and Prince Edward Regiment on mobilization in August 1939 with the rank of Captain and proceeded overseas as the regiment's Medical Officer. On his return, he was appointed Medical Officer of the Royal Canadian Artillery Training Centre at Petawawa. Later, he was Camp Medical Officer at Barriefield and became A.D.M.O. at Army Headquarters M.D. 3 in Kingston with the rank of Major. After receiving postgraduate training, he qualified as a specialist in radiology and was appointed Radiologist of the Recruiting Depot M.D. 3 at Fort Frontenac in Kingston.

From 1946 until his retirement in 1957, Dr. Leavens was Chief Radiologist of the Toronto Military Hospital. For the past three and one-half years, he was the Consultant Diagnostic Radiologist of the Port Hope and Cobourg General Hospitals and the Ontario Hospital at Cobourg.

Dr. Leavens was a Mason and a member of St. Mark's Anglican Church, Port Hope. He leaves his widow, the former Edith Box, and four children, Diana, Reg.N., of Toronto, Hudson at Queen's University, Richard and James of Port Hope and one brother, Harry, of Toronto.

DR. JOSEPH MILLAR, 61, died at his home in Toronto on April 19. A graduate of the University of Toronto Medical School in 1925, Dr. Millar had practised in Toronto for many years.

He is survived by his widow.

DR. STEPHEN F. MILLEN, 76, died May 5 at Woodslee, Ont., where he had lived and worked all his life. Known to his patients as "Doc", Dr. Millen was honoured in 1955 for his medical work in the community during the previous 50 years. Two thousand people attended the celebrations which were held at Woodslee Memorial Park.

Born on a farm between Cottam and Woodslee, he was educated at local schools and graduated from the University of Toronto Medical School in 1905. He spent one year working in Woodslee with his cousin, Dr. William H. Millen, and after his cousin moved, Dr. Millen carried on the practice until his death.

Dr. Millen was an honorary life member of the Essex County Medical Society. He had also been medical officer for Maidstone and Rochester Township for over 50 years. A few years ago Assumption University conferred on him an honorary degree of Doctor of Laws in recognition of his many years of service to the sick in his community.

Dr. Millen is survived by his widow, two daughters and a son, Dr. Donald Millen of Windsor, Ont.

DR. WILLIAM S. MURPHY, 79, former Member of Parliament and mayor of Smiths Falls, Ont., died April 29 in his home. Mayor of Smiths Falls from 1916 to 1918, Dr. Murphy was elected Conservative Member of Parliament in 1929 in a by-election. One year later he was defeated when he attempted to run as an independent Conservative.

Dr. Murphy is survived by his widow and two sons, Drs. Arthur B. Murphy and William O. Murphy.

DR. FREDERICK R. POLLOCK, 75, retired radiologist, died in Kitchener-Waterloo on April 14. Dr. Pollock had practised in Victoria, B.C., for several years before moving to Kitchener-Waterloo in 1926 to become resident radiologist at St. Mary's Hospital, Kitchener-Waterloo, Stratford General Hospital and Galt Hospital. He served overseas with the Canadian Army during World War I after graduating from the University of Toronto Medical School in 1916.

Dr. Pollock is survived by his widow, a daughter and a son, Dr. F. H. Pollock of Toronto.

DR. ALFRED L. RUSSELL, 86, died April 24 in Peterborough, Ont. Educated in Millbrook and the University of Toronto Medical School, where he graduated in 1905, Dr. Russell was another of Canada's horse and buggy pioneer doctors. His medical career began in his home town, Millbrook, where he worked for one year before going to Bailieboro. He practised in Bailieboro until his retirement in October 1960.

He is survived by his daughter.

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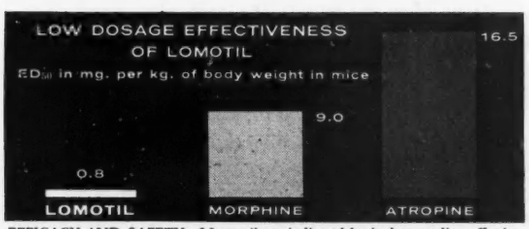

EFFICACY AND SAFETY of Lomotil are indicated by its low median effective dose. As measured by inhibition of charcoal propulsion in mice, Lomotil was effective in about 1/11 the dosage of morphine hydrochloride and in about 1/20 the dosage of atropine sulfate.

PRECAUTION: While it is necessary to classify Lomotil as a narcotic, no instance of addiction has been encountered in patients taking therapeutic doses. The abuse liability of Lomotil is comparable with that of codeine. Patients have taken therapeutic doses of Lomotil daily for as long as 300 days without showing withdrawal symptoms, even when challenged with nalorphine.

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DOSAGE: The recommended initial dosage for adults is two tablets (5 mg.) three or four times daily, reduced to meet the requirements of each patient as soon as the diarrhea is controlled. Maintenance dosage may be as low as two tablets daily. Lomotil, brand of diphenoxylate hydrochloride with atropine sulfate, is supplied as unscored, uncoated white tablets of 2.5 mg., each containing 0.025 mg. (1/2400 gr.) of atropine sulfate to discourage deliberate overdosage.

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Descriptive literature and directions for use available in Physicians' New Product Brochure No. 81 from

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June 24, 1961, vol. 84

PUBLIC HEALTH

SURVEILLANCE REPORT OF EPIDEMIC OR UNUSUAL COMMUNICABLE DISEASES

INFLUENZA

An outbreak of influenza-like illness has been reported from North West River, Happy Valley and Makkovik, all in Labrador. Several cases of secondary pneumonia have occurred among the Indian population. There have been three deaths, two in infants and one in an elderly Indian. The epidemic appears to be on the decline.

It has been reported from the County of Bellechasse, Quebec, that since the second week in April the incidence of influenza-like illness has greatly increased.

TRICHINOSIS

During the first two weeks in April, 5 more cases of trichinosis have been reported in Quebec, 4 in Montreal and 1 in Dorval.

Twenty-five cases of trichinosis were reported in the Province of Quebec for the first quarter of 1961.

TYPHOID FEVER

Five cases of paratyphoid fever due to S. *paratyphi B*, all in the same family, have been reported from the Moose Woods Indian Reserve, 13 miles south of Saskatoon, Sask. The first case occurred on February 27, 1961, and the other four on March 14. Water samples have been collected from the wells and T.A.B. vaccine has been given to all contacts, to school children and to all resident population. No additional cases have been reported since March 14.

INFECTIOUS HEPATITIS

Five cases of infectious hepatitis have been reported from Inuvik, N.W.T., bringing the total to 56 cases.

TETANUS

One case of tetanus in an adult male was reported in the city of Winnipeg for the week ended April 16, 1961.

PSITTACOSIS

One case of psittacosis has been reported from Lac du Bonnet, Man. The patient purchased a budgerigar in May 1960. The bird became sick and died in September. The patient first had chest pains last October and was admitted to hospital in January 1961.

International Reports

INFLUENZA

Connecticut becomes the second State to report influenza this year. (Cases of influenza A2 virus isolations were previously reported from New York City.) Influenza A2 was confirmed in three patients from Stamford late in February. In New Haven, influenza is occurring among university personnel, and isolations of the influenza A2 virus have been made.

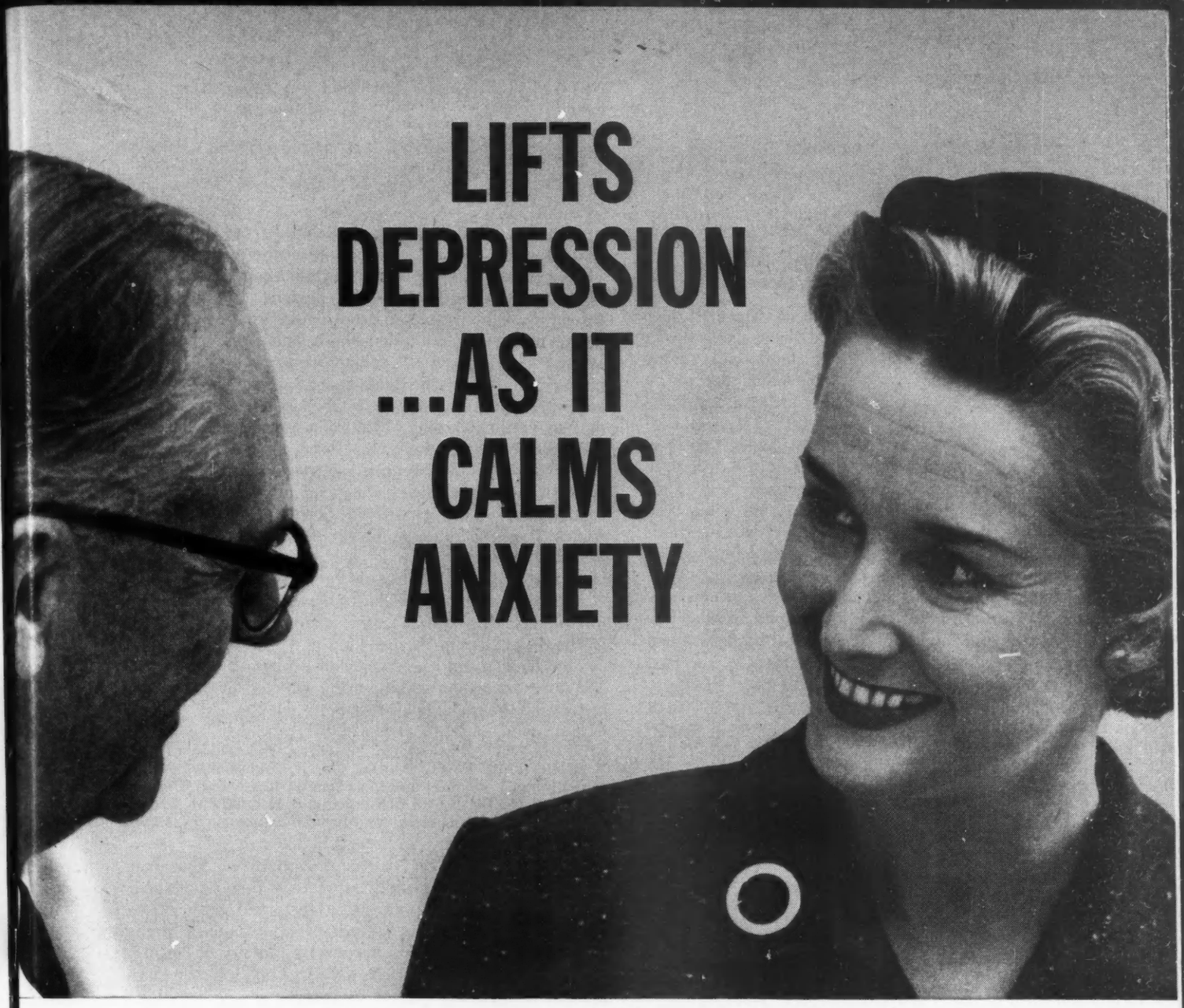
Epidemiology Division, Department of National Health and Welfare, Ottawa

April 22, 1961.

SUMMARY OF REPORTED CASES OF NOTIFIABLE DISEASES IN CANADA*
ISSUED BY THE PUBLIC HEALTH SECTION, DOMINION BUREAU OF STATISTICS

Disease	*Week ended (1961):* April 1	April 8	April 15	April 22	*Cumulative total since beginning of year* 1961	1960
Brucellosis (Undulant fever) (044)	3	1	1	3	27	18
Diarrhea of the newborn, epidemic (764)	9	2	—	—	27	15
Diphtheria (055)	—	1	2	—	33	10
Dysentery (045, 046, 048)	25	69	168	56	799	1,059
(a) Amebic (046)	—	—	—	—	5	1
(b) Bacillary (045)	14	11	126	22	405	945
(c) Other and unspecified (048)	11	58	42	34	389	113
Encephalitis, infectious (082.0)	—	—	—	—	—	—
Food poisoning: (049.0, 042.1, 049.2)	29	11	19	24	353	408
(a) Staphylococcus intoxication (049.0)	2	—	4	1	20	236
(b) Salmonella with food as vehicle of infection (042.1)	27	11	15	23	331	161
(c) Unspecified (049.2)	—	—	—	—	2	11
Hepatitis, infectious (including serum hepatitis) (092, N998.5)	184	218	269	209	3,796	2,142
Meningitis, viral or aseptic (080.2, 082.1)	2	1	5	5	49	66
(a) Due to Poliovirus	—	—	1	1	4	23
(b) Due to Coxsackie virus	—	—	—	—	3	1
(c) Due to ECHO virus	—	—	—	1	1	1
(d) Other and unspecified	2	1	4	3	41	41
Meningococcal infections (057)	6	5	2	3	54	58
Pemphigus neonatorum (Impetigo of the newborn) (766)	—	1	—	—	1	4
Pertussis (Whooping cough) (056)	71	61	123	79	1,248	2,070
Poliomyelitis, paralytic (080.0, 080.1)	—	2	4	2	22	81
Scarlet fever and Streptococcal sore throat (050, 051)	385	286	295	274	6,040	11,928
Typhoid and Paratyphoid fever (040, 041)	7	3	—	6	73	121
Venereal diseases (020-039)	249	303	305	362	5,513	5,054
(a) Gonorrhea (030-035)	208	266	281	326	4,840	4,457
(b) Syphilis (020-029)	41	37	24	36	672	594
(c) Other† (036-039)	—	—	—	—	1	3

*Figures for the Yukon are received four-weekly and are, therefore, shown in the cumulative totals only.
†Including chancroid, granuloma inguinale and lymphogranuloma venerum.



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BOOK REVIEWS

LIPIDS AND THE STEROID HORMONES IN CLINICAL MEDICINE. Edited by F. William Sunderman and F. William Sunderman, Jr. 207 pp. Illust. J. B. Lippincott Company, Philadelphia and Montreal, 1960. $10.75.

This book is a timely addition to the medical literature on lipids and steroid hormones. It discusses critically and briefly the practical laboratory methods available for the determination of various lipids and steroids in blood, feces and urine, and describes in detail a method of choice for each substance. In addition, the clinical interpretation of the results obtained with each method is given. The authors of each method and chapter are well selected, active investigators in their field. This book is of value to both the research worker and the practical hospital biochemist concerned with methodology, and also to the student interested in the description and significance of these lipid substances.

The serum lipid studies which are discussed include the following: extraction of lipids, total lipids, triglycerides, free and total cholesterol, total phospholipids and phospholipid fractionations, total fatty acids, free fatty acids and lipoproteins. The significance of these serum lipids in relation to atherosclerosis and diseases of lipid metabolism is ably discussed. The only exception is the apparent assumption by the authors of Chapter 8 that the presence of atherosclerosis is wholly dependent upon the serum lipoprotein spectrum.

One chapter concerns lipids in feces, their determination and their clinical interpretation.

The last 110 pages are devoted to the steroid hormones. This part begins with the fundamental chemical considerations of these steroids and the origin, distribution and measurement of their metabolites. The general methods described include colorimetric reactions, partition chromatography and use of radioisotopes. Specific methods are given for urinary 17-ketosteroids, corticosteroids, aldosterone and estrogens. In addition, methods for the measurement of plasma cortisol and adrenal cortical stimulation and suppression tests are included.

This reviewer highly recommends this book for those interested in the lipid and hormone fields. In fact I am tempted to keep for myself this copy of the book given to me for review, instead of presenting it to the library as suggested by the editor of the *C.M.A. Journal*.

(Editor's Note—By dint of Herculean effort the reviewer conquered his professed avarice and donated this volume to a medical library.)

THE RICKETTSIAL DISEASES. P. F. Zdrodovskii and E. H. Golinevich. 629 pp. Illust. Pergamon Press Inc., New York, London and Paris, 1960. $17.50.

This impressive treatise gives lucid and detailed descriptions of the complete range of rickettsiae pathogenic for man and the diseases caused by these agents. The accounts of the ecology of rickettsial diseases of the Soviet Union and neighbouring countries, many details of which are not readily available to investigators in the western hemisphere, are supplemented by a full bibliography. The authoritative note sounded by the authors both in their descriptions of epidemiology and laboratory procedures stems from their rich experience of personal investigations of rickettsial diseases over many years.

The English edition was translated from the Russian text of the second edition, published by Medgiz, Moscow, in 1956. In certain sections new material has been added, but the 1957 report of five laboratory infections which resulted from contamination of drains by Q fever was not mentioned. However, a comprehensive world picture of the ecology of Q fever included details of investigations in Uzbek, 1951, several central Asian republics in 1953 and the authors' own studies in the Ukraine, 1955. The excellent account of the epidemiology, vectors and laboratory characteristics of North Asian tick typhus contrasts sharply with the brief discussion of diseases caused by the antigenically related *Rickettsia conorii* in South Africa and East Africa. The recent appearance of further human cases of North Queensland tick typhus in southern Queensland and the slight antigenic relationship between this rickettsia and that of rickettsial-pox (*R. akari*) is not mentioned. However, a good account of rickettsial pox in the Soviet Union is provided.

This book should receive wide acclaim by physicians and other investigators who are interested in the natural history of the rickettsial diseases.

RESPIRATION. Physiologic Principles and Their Clinical Applications. P. H. Rossier, A. A. Buhlmann and K. Wiesinger. Edited and translated from the German Edition by Peter C. Luchsinger and Kenneth M. Moser. 505 pp. Illust. The C. V. Mosby Company, St. Louis, Mo., 1960. $15.75.

This book emphasizes the contributions of European investigators to the rapidly advancing field of respiratory physiology. The interesting historical basis of research in respiration is described and a great many references are given. The normal physiology of respiration is discussed in much detail. This section commences with an account of the mechanics of breathing which will confuse and discourage anyone not already conversant with this subject. The section on lung volumes uses some terms no longer employed in most laboratories. Some statements are very controversial, such as the definition of dyspnea as an increase in the work of breathing above the normal figure. The discussion on cyanosis is of considerable interest. The section dealing with techniques of measuring pulmonary function emphasizes spirometry and blood gas analysis, and varies from dealing with very simple details of spirometry to some very complex details of oximetry. It is strange to find only brief mention of popular modern techniques such as the Astrup method for measuring arterial blood carbon dioxide tension and carbon monoxide techniques for measuring diffusion capacity. Infra-red meters also receive scant attention, as does body plethysmography. The section on pathophysiology contains classifications of pulmonary insufficiency which most readers will find confusing. In the last section on pulmonary insufficiency in clinical practice there is much of interest, but again classifications, especially those involving emphysema, are confusing.

This book is of interest in that it is a survey of respiratory physiology from a European rather than a North American viewpoint. It is likely to be of value mainly to those investigators already concerned in research in respiration.

AIR POLLUTION. World Health Organization Monograph Series No. 46. 19 authors. 442 pp. Columbia University Press, New York, 1961. $10.00.

This book of over 400 pages is the culmination of efforts initiated by a panel of experts who attended a meeting of the Expert Committee on Environmental Sanitation of the World Health Organization in 1957. Each chapter is written by an authority in his respective field. The material included in the monograph contains a historical review and identification of the atmospheric pollution problem; an account of the role of meteorology; a discussion of methods of sampling, analysis and instrumentation; a presentation of some aspects of the physical and chemical nature of air pollution and the effects on health of man, animals and plants. Other chapters deal with economic and social aspects, prevention and control, and legislation. Radioactive pollution is discussed in the final chapter.

From the standpoint of medicine and biology, the acute and chronic effects of gaseous and aerosol contaminants on human health, animals and plants are obviously of major concern. Human health aspects are presented in a significant fashion in relation to both environmental and clinical findings from studies of major air pollution disasters and from reviews of symptomatology and pathology of specific pollutants, such as sulphur dioxide, ozone, airborne carcinogens, beryllium, manganese, carbon monoxide, insecticides, fluorides, allergenic agents and other substances. Consideration is given to the influences on health of reduced sunlight from air pollution, ingestion of pollutants, and odours.

This monograph is well written and represents a veritable storehouse of recent information on a subject that is rapidly assuming major importance. The literature in this field is vast and is growing constantly. Consequently, this contribution of the World Health Organization is both timely and useful to the medical practitioner, specialist or general reader interested in acquiring a quick grasp of the essentials of the air pollution problem. It should be welcomed as a valuable addition to any library.

THE UNDERGRADUATE TEACHING OF PSYCHIATRY AND MENTAL HEALTH PROMOTION. Ninth Report of the Expert Committee on Mental Health. World Health Organization Technical Report Series No. 208. 36 pp. World Health Organization, Geneva; Columbia University Press, New York, 1961. $0.30. Also published in French and Spanish.

This is the ninth report of the Expert Committee on Mental Health of the World Health Organization. It is a statement by this group of acknowledged experts of views on the undergraduate teaching of psychiatry. After a discussion of psychiatric development, within the framework of general medical education, it is concluded: "It cannot be doubted that the time has come for an appraisal of the role within the curriculum of psychiatry as a specialty and of psychiatry as an overall approach; this must be the main object of the present report" (page 6).

The Committee then proceed to do just this in a most interesting and thorough way. They point up the double role of psychiatry in medical education: (a) as a body of knowledge of personality functioning which is basic to the proper practice of all medicine; (b) as a body of specialized knowledge having to do with specific psychiatric problems.

A rather detailed statement of the content of the psychiatric curriculum and the hours needed by the psychiatric department is presented. This statement would be of great interest to the head of any psychiatric department on this continent. The point is made that psychiatric education will of necessity vary with the development of the local culture within which the medical school exists. Having stated this world viewpoint, it seems to this reviewer that the description of an ideal psychiatric curriculum is highly coloured by the North American viewpoint. Such complete coverage of the field seems to be necessary that even the head of a moderately progressive department of psychiatry on this continent may be pardoned for feeling that his own program is most inadequate. Were one studying the report with the object of initiating a new program in an under-developed area of the world, I am afraid one would so despair of achieving any worthwhile sort of standard that one would decide to go on leaving mental illness to the local witch doctors. To reiterate, for the North American professor of psychiatry wishing to check his undergraduate teaching against an ideal scheme, this is an excellent document. This reviewer would feel that a simpler statement emphasizing minimal requirements and what could be achieved with relatively meagre facilities would have been more appropriate.

Finally, a point is made several times which bears stating in full: "The student must be taught about the realistic limitations of psychiatric therapy. He must be informed that he will have to 'carry' many emotionally sick patients for indefinite periods with little apparent sign of improvement" (page 22). If such information were emphasized in many of our undergraduate and postgraduate teaching programs, our students' reality orientation would be closer to truth; and all of us in psychiatry would be less embarrassed by the unrealistic expectations which we sometimes foster.

LA GOUTTE. S. de Sèze et A. Ryckewaert avec la collaboration de J. Levernieux et R. Marteau. 268 pp. Illust. L'Expansion Scientifique Française, Paris, 1960. 47 NF. (approx. $9.25).

Cette monographie contient un exposé des progrès scientifiques de la diathèse hyperuricémique, des causes, du mécanisme et du traitement de la maladie. L'analyse des 180 cas observés par les auteurs est confrontée avec celle des cliniciens et chercheurs européens et américains. Des tableaux résument ces comparaisons statistiques de façon nette et concise. L'historique de la maladie dont on a une vue à vol d'oiseau dans le premier chapitre, est complété tout au long du livre par des notes supplémentaires. Les conditions d'apparition, la goutte aiguë, l'hyperuricie et l'hyperuricémie, les dépots uratiques avec photographies démonstratives, lésions radiologiques supplémentées de photos, discussion sur la lithiase rénale et la néphropathie goutteuse, les maladies d'accompagnement, l'évolution générale de la maladie, l'anatomie pathologique, une discussion sur la pathogénie de la goutte et le traitement des crises aiguës et de la période entre les crises sont les chapitres du livre suivis d'une bibliographie des travaux scientifiques aussi récents que 1959.

Cette monographie est d'une lecture facile et stimulante. L'aspect clinique de la maladie domine et le praticien général y trouvera toutes les connaissances nécessaires pour reconnaître et traiter la goutte.

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HEALTH IN CHILDHOOD. Richard W. B. Ellis. 251 pp. Illust. Penguin Books Ltd., Harmondsworth, Middlesex; Longmans, Green & Company, Toronto, 1960. $1.00.

As is stated in the foreword, Professor Ellis has attempted to set forth the complex picture of the developing child and outline the factors which determine the physical, mental and emotional health of the child. In this Professor Ellis has been eminently successful, and his book is written in a lucid and readable fashion without suffering from oversimplification. The book is divided into eight chapters which trace the child's development from conception through birth and infancy to puberty. The first two chapters cover health and disease as influenced by the child's environment, both in the family and in the community, related to his age, constitution, immunity and so forth. The environmental and genetic factors are further elucidated in the child before birth, during birth and subsequently. Two chapters are devoted to nutrition and feeding and to growth and development, respectively. The final chapter discusses physical and mental handicaps and emotional maladjustment. While setting forth the factors affecting health and development of the child in a factual manner, in so far as these are understood, the author's personal philosophy on many problems comes to the fore. The author makes many statements which should provoke thought. For instance, on productive work he states, "However desirable ten years' formal education may be for the majority of children (and its desirability for all is by no means proven), it has led in practice to considerable neglect of one aspect of the child's normal development", i.e. the increasing capacity of an older child for productive work. Of the Western model of universal formal education, he points out that it is important to recognize that the more advanced countries have been notably more successful in improving the general level of health of the childhood community than they have in eliminating emotional maladjustment. He feels that the deflation of the father figure in modern society may at least be partly responsible for the present problems of adolescent youth. Of the birth process he states, "Although it is often piously suggested that birth is an essentially normal process which should hold no terrors for the healthy woman, it is more realistic to regard it as a natural hazard which is made more or less difficult by human agency and which is successfully negotiated by the great majority of infants and their mothers."

This book is not intended as a ready reference for diseases of children or the management of their various problems. It is essentially a broad statement which should give serious-minded parents a deeper insight into factors affecting their child's development. For the first- or second-year medical student, it would serve as an excellent introduction to health and disease in childhood, giving him a broad outlook towards problems he will encounter later in his career. Similarly, for doctors who have not had any formal pediatric training, as, for example, ancillary workers in the medical field who work with children, it would be a valuable book to read. For the more advanced student or experienced physician the material is presented in more detailed form in standard texts. Indeed, Professor Ellis borrows heavily from his textbooks on Child Health and Development, and Disease in Infancy and Childhood. In all, this is excellent value for $1.00.

THE MATHEMATICS OF MEDICINE AND BIOLOGY. J. G. Defares and I. N. Sneddon. 663 pp. Illust. The Year Book Publishers, Inc., Chicago, Ill., 1960. $14.00.

The fact that medical and biological journals contain an ever-increasing number of articles which make use of mathematical procedures has led to the publication of this book. It should be pointed out that this is not a text in statistics or statistical methods; actually the theory of statistics is not included. On the other hand, the book presents all the basic tools which are necessary for the study of the elementary theory of mathematical statistics. A goodly number of examples are included and these are chosen from various areas of physiology, pharmacology and clinical medicine, each example illustrating certain mathematical procedures. The actual content of the book covers the mathematical field from elementary algebra through trigonometry and differential calculus to differential equations. To the reader with limited mathematical training this may appear formidable, but since the mathematical tools are developed against a biological background they can be mastered, though perhaps only with extensive use of paper and pencil. The book is primarily designed, however, for senior personnel in the medical and biological sciences who desire a review of mathematical principles and their application.

FUNCTIONAL NEURO-ANATOMY. Including an atlas of the brain stem. 4th ed. A. R. Buchanan. 377 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1961. $8.50.

The fact that a new edition of this textbook has been necessary only four years after the appearance of its predecessor is, perhaps, sufficient evidence of its continuing popularity with medical undergraduates, for whom it is written.

As a result of recently acquired knowledge, the author has found it necessary to expand his description of the thalamus, and his references to the reticular formation and the reticular activating system have been expanded from those of the third edition.

The bibliography has been lengthened, but the text has been kept to within a few pages of its previous length. The diagrammatic line-illustrations of functional nerve-pathways are good and the attractive format has been retained.

KLINISCHE CHIRURGIE FUER DIE PRAXIS. Band III, Lieferung 3. Edited by O. Diebold, H. Junghanns and L. Zukschwerdt. 581 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1961. $9.75.

There are three excellent monographs in this instalment of the *Clinical Practice of Surgery* series. The first presents a discussion of diseases, injuries and malformations of the small bowel, with an additional chapter on bowel obstruction. The second covers a similar field with reference to the colon, and the third deals with the subject of appendicitis.

The description of different methods of clinical examination and the adequate and lucid discussions of anatomy and pathophysiology follow the pattern set in the other volumes of this series. Like the previous instalments, this book is up to date and contains ample references to the current literature.

This section is a very useful and valuable component of the *Clinical Practice of Surgery* series.

MEDICAL NEWS *in Brief*

(Continued from page 1452)

DARLING FOUNDATION MEDAL AND PRIZE

The Darling Foundation Medal and Prize for contributions to research in malaria has been awarded by the World Health Organization jointly to Major-General Sir Gordon Covell, formerly of the Indian Medical Service and director of the Malaria Reference Laboratory (Medical Research Council), Horton Hospital, Epsom, and adviser on malaria to the Ministry of Health, and to Dr. Arnoldo Gabaldon, of Venezuela. The prize was presented at the Fourteenth World Health Assembly.

Sir Gordon, who was born in 1887, was educated at King's School, Canterbury, and Guy's Hospital, London. He is late director of the Malaria Institute of India, and was honorary physician to King George VI. He was appointed C.I.E. in 1939, and knighted in 1946.

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COURSE IN LARYNGOLOGY AND BRONCHOESOPHAGOLOGY

The Department of Otolaryngology, University of Illinois College of Medicine, will conduct a postgraduate course in Laryngology and Bronchoesophagology from October 23 to November 4, 1961, under the direction of Paul H. Holinger, M.D.

Registration will be limited to 15 physicians who will receive instruction by means of animal demonstrations and practice in bronchoscopy and esophagoscopy, diagnostic and surgical clinics, as well as didactic lectures.

Enquiries should be directed to the Department of Otolaryngology, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12, Illinois.

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THE DORIS ODLUM PRIZE IN THE FIELD OF MENTAL HEALTH

The British Medical Association announces that the Doris Odlum Prize, for studies in the field of mental health, will be awarded in 1962 for a study of "Progress in the Community Care of Mental Disorder": critical and constructive review of advances made in this field in the five years ending on September 30, 1961. The prize is of £80 in value. Any medical practitioner registered in the British Commonwealth or in the Republic of Ireland may compete.

Preliminary notice of entry is required. Forms and further particulars may be obtained from The Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1. The closing date for entries is December 31, 1961.

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SECOND MIDDLE EASTERN-MEDITERRANEAN PEDIATRIC CONGRESS

The Second Middle Eastern-Mediterranean Pediatric Congress will be held in Ankara, Turkey, from September 6 to 9, 1961, under the sponsorship of the Ministry of Health and Social Assistance, the National Society of Pediatrics and Child Health of Turkey, the Turkish Pediatric Association, the Ankara Child Health Society and the Research Institute of Child Health of Ankara University. Official languages of the Congress will be English, French and Turkish.

For information, address communications to: The Secretary General, Second Middle Eastern-Mediterranean Pediatric Congress, Hacettepe Cocuk Hastahanesi, Ankara, Turkey.

TENTH INTERNATIONAL CONGRESS OF PEDIATRICS

The Tenth International Congress of Pediatrics will take place in Lisbon, Portugal, from September 9 to 15, 1962. Scientific meetings will be held in the buildings of the University City of Lisbon.

Registrations will be accepted after August 1, 1961. From February 1, to May 31, 1962, the registration fee will be increased by 25%. No registrations will be accepted after May 31, 1962. Bulletins of registration and preliminary programs will be sent to national pediatric associations for distribution to their respective members.

The address of the Congress Secretariat is as follows: Tenth International Congress of Pediatrics, Clinica Pediatrica Universitaria, Hospital Santa Maria, Av. 28 de Maio, Lisboa 4, Portugal.

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FOURTH INTERNATIONAL CONGRESS OF ALLERGOLOGY

The Fourth International Congress of Allergology will be held at the Hotel Commodore, New York City, from October 15 to 20, 1961. This congress is under the auspices of the International Association of Allergology. Dr. Bernard N. Halpern, President of the Association, will be President of the Congress, and Dr. Francis B. Rackemann will be Honorary President. All physicians and scientists who register will be members of the Congress, regardless of previous membership in the Association. The Chairman of the Organizing Committee is Dr. William B. Sherman, 60 East 58th Street, New York 22, New York, U.S.A. All communications should be directed to him.

The registration fee for members will be $45.00 which will include the published Proceedings of the Congress. Registration for wives and non-medical guests accompanying the members will be $20.00. These registration fees will include admission to the receptions but the banquet will be charged separately. It is essential that those desiring to offer papers at the Congress REGISTER NOW to allow time for publication of the abstracts.

The principal meetings will be held at the Commodore Hotel, which will be the headquarters of the Congress. This hotel is conveniently located and will offer excellent accommodations. The hotel will attempt to reserve an adequate number of rooms for those

(Continued on page 26)

MEDICAL NEWS *in brief*

(Continued from page 25)

attending the Congress, but it is desirable that definite reservations be made now in order to secure accommodations desired.

The official languages of the Congress are English, French, German and Spanish. Papers may be presented in any of these four languages. The symposia will be simultaneously translated into the other official languages by expert medical interpreters so that the members can follow the reports and participate in the discussions.

AMERICAN PUBLIC HEALTH ASSOCIATION 89TH ANNUAL MEETING

The 89th annual meeting of the American Public Health Association and meetings of about 60 related organizations will be held at Cobo Hall in Detroit, Mich., November 13-17, 1961. Registration will be open to non-members.

Among those attending will be administrators, research scientists and other specialists on the staffs of international, national, state and local health services and voluntary agencies.

Scientific sessions and exhibits will cover community health, prevention of disease and control of environmental health factors. The association's fourteen sections, each of which will hear progress reports from outstanding researchers and practitioners, represent dental health, engineering and sanitation, epidemiology, food and nutrition, health officers, laboratory, maternal and child health, medical care, mental health, occupational health, public health education, public health nursing, school health and statistics.

Joseph G. Molner, M.O., health commissioner of Detroit, is chairman of the local arrangements committee.

POSTGRADUATE COURSE ON EMERGENCIES IN GENERAL PRACTICE

A postgraduate course on "Emergencies in General Practice", sponsored by the Medical Alumni Association of the University of Toronto, will be given at Sunnybrook Hospital, Toronto, on October 11, 12 and 13, 1961. No advance registration is required. Credits will be given members of the College of General Practice on an hour-for-hour basis of actual lecture time.

CANADIAN SOCIETY FOR THE STUDY OF FERTILITY

The eighth Annual Meeting of the Canadian Society for the Study of Fertility will take place at the Sheraton Brock Hotel, Niagara Falls, Ontario, on October 27 and 28, 1961.

Further information may be obtained by writing to the Secretary, Dr. George H. Arronet, Infertility Centre, Royal Victoria Hospital, Montreal.

HEART DISEASE IN U.S.

Currently at least 5¼ million people in the United States have known heart conditions, and four-fifths of them are 45 years of age or older, according to statisticians of the Metropolitan Life Insurance Company.

This estimate is based on data collected in household interviews by the U.S. National Health Survey. Metropolitan statisticians point out that even this large figure is an understatement of the actual prevalence

of the disease, since the survey related only to persons who were aware of these heart conditions.

The relative frequency of heart trouble increases sharply with advance in age, the survey indicated. For example, under age 25 approximately 5 males per 1000 of population have some kind of heart ailment. By ages 45 to 54, the rate is 39 per 1000, and it then rises rapidly to 85 per 1000 at ages 55 to 64, and to 140 in the 65-74 age group. Heart conditions are more common among men than among women, except at ages 75 and over.

"The pattern of mortality from heart disease in the United States is similar to that for morbidity," Metropolitan statisticians noted. "The death rate from the disease is the lowest among children of school age and rises very rapidly thereafter with advance in age."

Indicating that heart disease will undoubtedly continue to be a major medical and public health problem, the statisticians concluded:

"The main tasks therefore are to prevent premature illness and death from the disease, to improve the care and management of cardiac patients, and to rehabilitate them to their greatest potential.

"Life insurance mortality investigations have consistently shown that overweight and elevated blood pressure are associated with excessive mortality from heart disease in middle and later life. These findings underscore the importance of weight control in both the prevention and management of heart disease."

SECOND CANADIAN MENTAL HEALTH SERVICES INSTITUTE

The Second Canadian Mental Health Services Institute, sponsored by the Canadian Psychiatric Association, will be held in the Château Laurier, Ottawa, January 15-18, 1962. The theme of the conference will be "Mental Health Services for Canada" — an examination of the 1961 C.M.H.A. report. Further information is available from: Dr. V. E. Chase, Chairman, Planning Committee, c/o C.P.A., Suite 103, 225 Lisgar Street, Ottawa, Ontario.

COURS DE CARDIOLOGIE AUX MEDECINS PRATICIENS

Un cours de cardiologie aux médecins praticiens aura lieu à l'Institut de Cardiologie de Montréal, du lundi 20 Octobre au samedi 4 Novembre 1961. Les invités d'honneur sont les docteurs Léon Gallavardin, cardiologue, et Pierre Michaud, chirurgien, de Lyon, France.

Le programme se composera de: Quatre démonstrations cliniques: Auscultations des lésions valvulaires acquises et des malformation congénitales; Six conférences: (1) La phonocardiographie: précisions qu'elle peut apporter à l'auscultation et au diagnostic, (2) L'arythmie complète. Forme permanente et forme paroxystique. Conduite à tenir, (3) Diagnostic d'une syncope par le docteur Léon Gallavardin, et (1) Apport de l'angiocardiographie sélective dans le diagnostic et les indications opératoires de certaines cardiopathies congénitales et acquises, (2) L'hypothermie profonde associée à la circulation extra-corporelle dans la chirurgie à ciel ouvert, (3) Les possibilités chirurgicales dans le traite-

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ment chirurgical de l'insuffisance mitrale par le docteur Pierre Michaud. Huit panels: (1) Diagnostic et traitement da la fièvre rhumatismale, (2) Classification et diagnostic des malformations congénitales, (3) La chirurgie des malformations congénitales, (4) Traitement de l'hypertension artérielle, (5) Traitement de l'insuffisance cardiaque, (6) Diagnostic de la maladie coronarienne, (7) Traitement de la maladie coronarienne. (8) La chirurgie des lésions valvulaires. Cinq forums: Réponses aux questions des auditeurs.

Le montant de l'inscription est de cinquante dollars. Toute correspondance doit être adressée à l'adresse suivante: Cours de cardiologie, a/s Dr Paul David, Institut de Cardiologie de Montréal, 5415, Boulevard de l'Assomption, Montréal 36.

CANADIAN LIFE INSURANCE MEDICAL FELLOWSHIP FUND AWARDS

Financial assistance from the Canadian Life Insurance Medical Fellowship Fund has been granted to 15 medical research workers at 11 medical schools of Canadian universities. The aggregate amount awarded by the Fund this year is more than $84,000. Seven of the 15 fellowships are for new investigations; the other eight are renewals from previous years.

Receiving fellowships are the following: Dr. L. J. Clein, University of Alberta, for continuation of his research on experimental and clinical therapy in irreversible shock; Dr. W. P. Warren, Dalhousie University, for continuation of research on carbohydrate metabolism in obesity; Dr. Guy Lamarche, Laval University, for research on sensory connections to the reticular formation of the brain stem; Dr. S. S. Parmer, University of Manitoba, for study of the mechanisms of drug action; Dr. R. F. P. Cronin, McGill University, for continuation of his heart research project; Dr. J. M. McKenzie, McGill University, for continuation of his study of the pathogenesis of hyperthyroidism; Dr. D. A. Hillman, McGill University, for continuation of his study of adrenal function in the newborn infant; Dr. J. R. Ducharme, University of Montreal, for continuation of his research on adrenocortical function in premature and newborn infants, infancy and childhood, and for comparative studies of the pattern of C_{21} and C_{19} steroid excretion with maturation; Dr. V. M. Napoli, University of Ottawa, for studies on hemophilia; Dr. P. de Bellefeuille, University of Ottawa, for continuation of his critical evaluation of previous perinatal studies; Dr. Jean-Marie de Margerie, Queen's University, for continuation of his study of the retinal vasculature in hypertension; Dr. T. Amemori, University of Saskatchewan, for study of the factors which influence cholesterol metabolism; Dr. D. R. Wilson, University of Toronto, for research on the diagnosis of renovascular hypertension; Dr. I. A. Korman, University of Toronto, for study of intestinal malabsorption and motility; and Dr. L. L. De Veber, University of Western Ontario, for research on immunohematology and pediatric hematology.

8th INTERNATIONAL CANCER CONGRESS – MOSCOW, JULY 22-28, 1962

The Eighth International Cancer Congress will take place in Moscow from July 22 to 28, 1962, under the auspices of the International Union

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Against Cancer. The Congress will meet at the Moscow State University.

Problems concerning cancer will be approached at the Congress from both experimental and clinical aspects.

The registration fee is 30 U.S. dollars per member, if sent before April 1, 1962.

Foreign members of the Congress will be served by the Soviet travel agency "Intourist". Applications for reading papers will be considered only on condition that both the application and abstract of the paper (not exceeding 250 words) are submitted not later than November 1, 1961.

All information concerning the Congress, as well as enrolment forms and applications to read papers and show cinematograph films, may be obtained through the Secretariat of the Soviet National Organizing Committee of the 8th International Cancer Congress at the following address: General Secretary of the Soviet National Organizing Committee—Prof. L. Shabad; or Assistant General Secretary—Dr. N. Perevodchickova, Academy of Medical Sciences of the U.S.S.R., 14, Solyanka, Moscow, U.S.S.R.

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11th ANNUAL INSTRUMENT SYMPOSIUM AND RESEARCH EQUIPMENT EXHIBIT

The 11th Annual Instrument Symposium and Research Equipment Exhibit will be held at the National Institutes of Health, Bethesda, Maryland, from October 9 to October 12, 1961. The Symposium and the Exhibit are sponsored by the Washington Sections of the American Association of Clinical Chemists, the American Chemical Society, the Instrument Society of America, the Society of American Bacteriologists, the Society of Applied Spectroscopy, and the Society for Experimental Biology and Medicine.

Primary topics for discussion on the scientific program include: (1) Applied Gas Chromatography; (2) Factors Influencing Interpretation of Spectra; (3) Electron Magnetic Resonance; (4) Thermogravimetric Analysis; (5) Electron Probe Analysis; (6) Application of Physiological Instrumentation to Clinical Problems; and (7) Optical Rotatory Dispersion.

Examples of the latest types of research equipment will be exhibited by instrument manufacturers.

Further information from: James B. Davis, Executive Secretary, National Institutes of Health, Bethesda 14, Maryland.

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TENTH INTERNATIONAL CONGRESS OF CATHOLIC DOCTORS

The Tenth International Congress of Catholic Doctors will be held in London, England, July 9 to July 13, 1962. The theme will be: "The Catholic Doctor in a Changing Society", under the following headings: The Adolescent, The Hopeless Case, The Ageing Population, Mental Health, Medicine in the Newly Independent Countries. Four papers will be presented at each session; the principal paper is not to exceed 30 minutes and the other contributions not more than 20 minutes.

Catholic doctors from Canada are invited to attend the Congress and to present papers on the various subjects. All communications should be addressed to the Secretary, Dr. J. W. Dignan, 58, Sebert Road, Forest Gate, London, E.7, England.